

# *The American Journal of* **DIGESTIVE DISEASES**

*An Independent Publication*

**DEVOTED TO GASTRO-ENTEROLOGY AND NUTRITION**

ORIGINAL CONTRIBUTIONS

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Volume 21

January, 1954

Number 1

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### *References:*

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3. Metcalf, R.G.: J. Maine M. A. 44:183 (July) 1953

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Best, R. R.; Hicken, N. F., and Finlayson, A. I.: *Ann. Surg.* 110:67, 1939.

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Beckman, H.: *Pharmacology in Clinical Practice*, Philadelphia, W. B. Saunders Company, 1952, p. 361.

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O'Brien, G. F., and Schweitzer, I. L.: *M. Clin. North America* 37:155 (Jan.) 1953.

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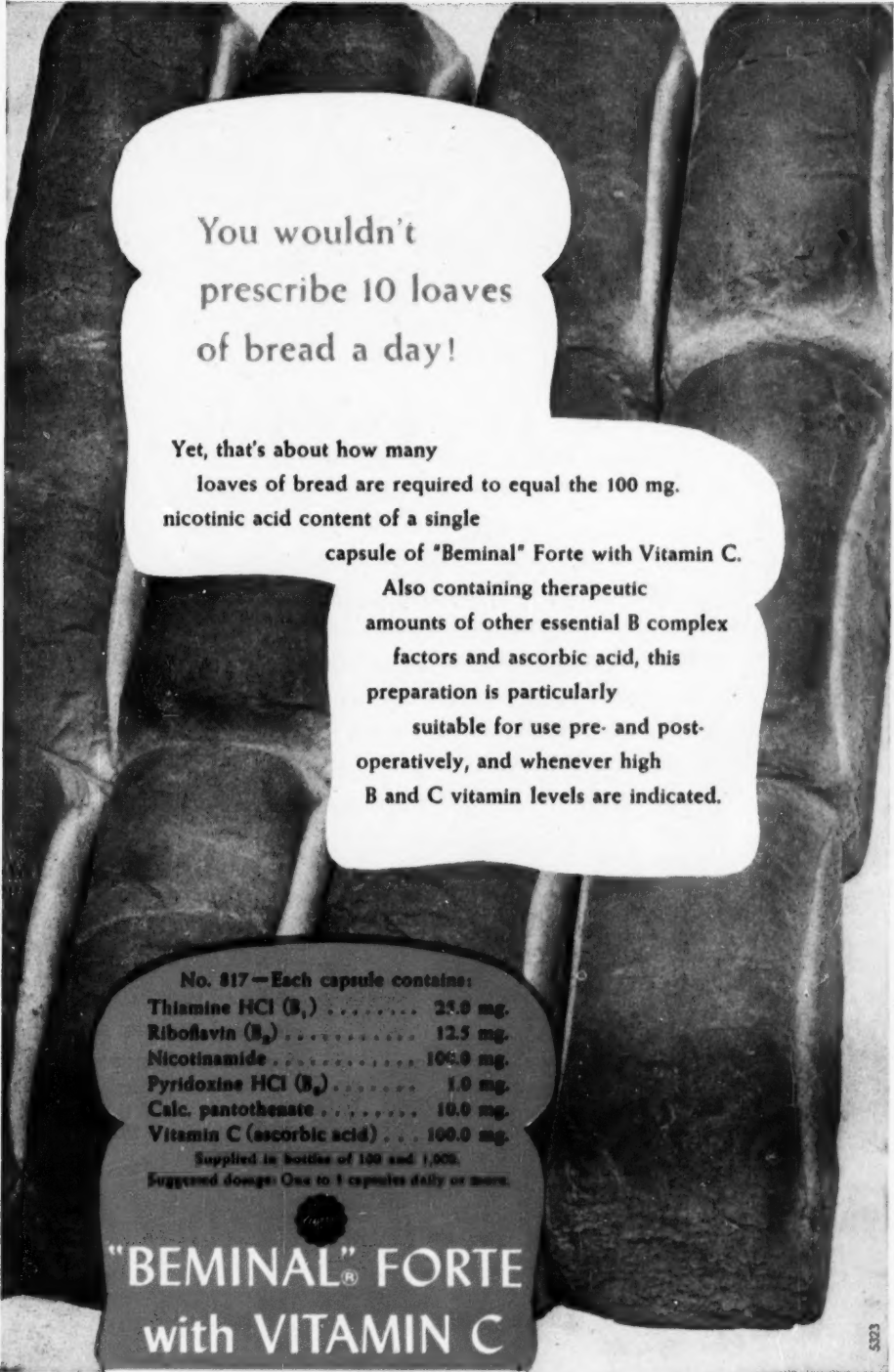
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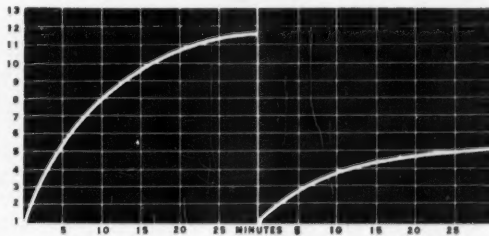
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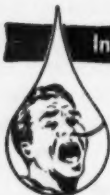
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# THE INCREASED ANTACID EFFECT OF ALUMINUM HYDROXIDE COMBINED WITH MAGNESIUM TRISILICATE

S. HYMAN, M. D., L. L. HARDT, M. D. AND F. STEIGMANN, M. D., Chicago, Ill.

**C**OLLOIDAL aluminum hydroxide was first introduced for the treatment of peptic ulcer somewhat over twenty years ago (1, 2). In the stomach it neutralizes HCl forming aluminum chloride and water. It acts more slowly than the soluble alkalis and raises the pH to only about 3.5-4 (at which level Topfers indicator is negative). It possesses adsorbent properties toward many substances, but absorbs hydrogen ion only to a limited extent. Because of its lack of alkaline character, it was considered not to cause a reactive secretion of HCl (acid rebound) and because it is practically unabsorbable from the alimentary tract, it is believed not to disturb the pH balance of the system (no possibility of alkalosis). Some believe that the aluminum ion inhibits pepsin activity even in acid solution. Besides its antacid effect, it is protective and astringent. It also interferes with the absorption of phosphorus from the alimentary tract and may thus cause phosphorus deficiency in the presence of associated diarrhea or pancreatic deficiency. It has to be given in large doses hourly to raise the pH and as with other antacids, a tendency to a secondary rise in acidity has been noted by some observers.

Numerous clinical reports as cited from the literature by Batterman and Ehrenfeld (3) attest to the value of aluminum hydroxide gel in the treatment of peptic ulcer. The main disadvantage of aluminum hydroxide treatment in peptic ulcer is its constipating effect. Thus, some (4) report constipation of variable degree in 17 to 59 percent of their patients while some found actual fecal impaction (5). The addition of antispasmodics or mineral oil decreased but did not eliminate the constipating effect (3). The constipating effect was similarly noted with the non-reactive aluminum hydroxide gels (3). This latter observation is at variance with the accepted teaching that the constipation with aluminum hydroxide is the result of the formation of astringent aluminum chloride.

Magnesium trisilicate was introduced by Mutch in 1925, as an antacid for the treatment of peptic ulcer and several reports attested to its value (6). Other reports, however, were less enthusiastic about this substance as the sole antacid in the treatment of peptic ulcer patients, pointing out that to achieve relief of ulcer symptoms, large doses (1-5 gm.) every four hours are needed (3) and that such doses usually resulted in increased intestinal irritation as evidenced by borborygmus, abdominal colic and laxation.

Since the clinically desirable antacid effects of aluminum hydroxide preparations were occasionally overshadowed by their attendant, undesirable side effect—constipation—it was thought that a combination of

these substances with the weaker antacid—magnesium trisilicate—which had a laxative side effect, might provide a more ideal antacid mixture. A number of such mixtures are now available and some reports (7) seemed to indicate the usefulness of such medication in the treatment of peptic ulcer.

In this paper, an attempt has been made to evaluate the effectiveness of some of the magnesium trisilicate-aluminum hydroxide mixtures, both from the purely antacid and from the clinical point of view. Five substances given in varying dosages were tested: Hypercin\* (2 and 4 tablets), Pink Alkajel\*\* (2 and 4 tablets), Gelusil\*\*\* (2 tablets), Mag-Sal\*\*\*\* (2 tablets) and AMT\*\*\*\*\* (2 tablets).

## MATERIAL AND METHOD

### *Peptic ulcer (gastric and duodenal).*

Patients in the wards and in the out-patient gastrointestinal clinic of the Cook County Hospital, and a small number of private patients were studied. All patients who were studied clinically, were recurrent chronic ulcer cases who were treated with one of the preparations during a recurrence of their symptoms. The majority of them were treated with one of these substances (Hypercin) because we were particularly interested in the therapeutic claims made for this latter material.

For the antacid study only hospitalized patients were used.

*A. Antacid Study:* Our method of testing the antacid drugs consisted of comparing the degree of gastric acidity obtained following histamine injection alone, with that obtained following histamine injection plus the ingestion of the substance to be tested. The fasting patients were intubated with a Levine tube and their gastric contents were completely evacuated. Thereafter, they were aspirated at 15 minute intervals until three additional samples were obtained. After the fourth sample was obtained, the subjects were given 0.1 mgms. of histamine per 10 kilo weight, and the aspirations were continued every 15 minutes for another 75 minutes. On the next day, this technique was repeated. However, at this time, the subjects were given an antacid by mouth simultaneously with the histamine injection. Aspirations were continued as on the previous days.

\*Each tablet contains magnesium trisilicate 0.3 gm. and aluminum hydroxide 0.6 gm.

\*\*Each tablet contains 0.3 gm. aluminum hydroxide and 0.6 gm. magnesium trisilicate.

\*\*\*Each tablet contains magnesium trisilicate 0.5 gm., and partially dehydrated aluminum hydroxide gel corresponding to 0.26 gm. of aluminum hydrate.

\*\*\*\*Each tablet contains 0.64 gm. aluminum hydroxide and 0.1 gm. magnesium trisilicate.

\*\*\*\*\*Each tablet contains 0.15 gm. aluminum hydroxide and approximately 0.25 gm. of magnesium trisilicate.

From the Departments of Internal Medicine and Therapeutics, and the Gastro-Intestinal Clinic of the Cook County Hospital, Chicago, Illinois.

Supported by grants from the Hardt Foundation and the Consolidated Royal Chemical Corporation, Chicago, Illinois.

Submitted May 28, 1953.

*B. Clinical Study:* Of the fifty patients with peptic ulcer (7 gastric, 1 prepyloric, 2 marginal, and 40 duodenal) who were observed clinically for the therapeutic effect of Hypercin, all had had symptoms from one to many years and had been on diet and various medications previously with intermittent improvement. Some of them had associated diseases (e.g. four had colitis, one had a myocardial infarction, one had renal stones, one had gallbladder disease, and one had rheumatoid arthritis). Four had slight pyloric obstruction, two had had previous bleeding, one had perforated previously, and two had had gastric subtotal resections.

Of the 50 cases, three were under observation for only two weeks, four for two months, seven for three months, eight for four months, four for five months, six for six months, two for seven months, one for eight months, four for nine months, three for twelve months, two for 14 months, four for 15 months, one for 16 months and one\* over two years. All patients were given two tablets four times daily (one hour after meals and at bedtime) in addition to an ambulatory ulcer diet, sedatives, and anti-spasmodics. Five patients received six tablets every two hours during the first week, and then, upon improvement of symptoms, were put on two tablets four times daily. The patients were seen at first, weekly, then every two weeks, and then, once a month if symptoms were minimal. At each visit, the patients were asked about any gastro-intestinal symptoms (appetite, nausea, pyrosis, vomiting, constipation, diarrhea) or other complaints. In some, especially the gastric ulcer cases, repeat x-rays were taken at various intervals. Some of these patients also had gastroscopic studies before and during the period of observation.

\*This patient had been taking Hypercin for about nine months when first seen by one of us for an upper respiratory infection.

## RESULTS

*A. Laboratory Studies:* The antacid effect of all the tested drugs appeared to be similar. A significant antacid effect was produced by Hypercin, Mag-Sal, Gelusil, and A.M.T. while Pink Alkajel (2 tablets and 4 tablets) had a somewhat lesser effect (Table 1) (Graph 1).

These substances compare favorably in antacid qualities with most of the highly effective antacids studied and reported in a previous paper (8). Two tablets of Hypercin produced a moderate acid neutralizing effect. Four tablets of Hypercin produced a greater and longer lasting antacid effect. The best effect was produced by two tablets of Hypercin repeated at 60 minute intervals.

*B. Clinical Studies:* The therapeutic results obtained with Hypercin were essentially similar to those obtained with other antacid substances in ulcer patients. Thirty-four of the patients had a decrease of their symptoms shortly after taking Hypercin and continued to improve so that they became symptom-free within variable lengths of time. These patients continued to do well, and were, therefore, classified as improved cases during the period of observation. The seven gastric ulcer patients fell in this group. X-ray revealed that every one had been healed. The time required in each case differed.

Of these 34 patients, one had a recurrence of symptoms six months later following a severe, emotional upset, and one had a recurrence of stomach symptoms in association with an exacerbation of her amebic colitis. Six of these patients were symptomfree despite taking the medication only intermittently after the first few weeks. One patient, however, noted gastric symptoms soon after stopping the medication and hence,

TABLE I  
DIFFERENCE IN FREE ACIDITY MEASURED AT FIFTEEN MINUTE INTERVALS  
WHEN HISTAMINE ALONE AND HISTAMINE PLUS ONE OF THE TEST  
SUBSTANCES WAS ADMINISTERED

Chemical Composition	Trade Name	Dosage	No. of Cases	Time in Minutes after Giving Histamine and Antacid				
				15	30	45	60	75
Aluminum Hydroxide	Amphojel	Two Tablets	10	-21	-8	+3	+15	+8
Aluminum Hydroxide and Magnesium Trisilicate		Two Tablets	27	-27	-9	+7	+1	+6
Aluminum Hydroxide and Magnesium Trisilicate	Hypercin	Four Tablets	17	-36	-15	0	-5	+1
Aluminum Hydroxide and Magnesium Trisilicate		2 Tab. at 1 Hr. Intervals	11	-36	-39	-24	-17	-24
Aluminum Hydroxide and Magnesium Trisilicate	Pink Alkajel	Two Tablets	6	-16	-26	-16	-9	+8
Aluminum Hydroxide and Magnesium Trisilicate		Four Tablets	7	-21	-29	-11	-13	+6
Aluminum Hydroxide and Magnesium Trisilicate	Gelusil	Two Tablets	10	-40	-41	-46	-26	-19
Aluminum Hydroxide and Magnesium Trisilicate	Mag-Sal	Two Tablets	10	-46	-46	-42	-6	+2
Aluminum Hydroxide and Magnesium Trisilicate	A.M.T.	Two Tablets	11	-38	-28	-5	-22	-11

started it again promptly. One of these patients stated that this medication gave him much more relief than powders. Three patients stated that they were slightly constipated.

Thirteen patients had only slight relief of their gastric symptoms. In analyzing this group, it was found that it comprised mainly the patients who had associated disease (coronary sclerosis, renal stones, amebic colitis, arthritis, marginal ulcer, and slight pyloric obstruction.) One of these patients had a prepyloric ulcer. In several of these patients, the emotional factor was also quite marked and was probably the reason for the poor cooperation in carrying out a strict therapeutic regimen. Thus, nine patients admitted that they took the medication more or less intermittently, despite the fact that they felt better during the period of regular medications. One patient developed a severe hemorrhage while on therapy and had to have a sub-total gastrectomy. Four patients complained of constipation. One patient became worse during an exacerbation of his amebic colitis.

Three patients stopped the medication after two weeks trial because of intolerance to taste, although they stated that the medication helped their gastric symptoms.

#### GASTROSCOPIC STUDIES

A number of patients who had x-ray findings of gastric ulcers and in whom the lesion was seen gastroscopically, received two tablets of Hypercin or of Gelusil crushed to a coarse powder, after the local anesthesia of the oropharynx had worn off. Later, some of these patients were regastroscooped at 30 minutes, others at 45 minutes, and still others, at 60 minutes, in order to see the local effect of these substances on the ulcer. In most of the patients, particles of either substance were seen clinging to the mucosa throughout the stomach. At times these particles were collected into clumps and gave a picture similar to milk curds adhering to the wall. These particles or clumps were

noted between and on the rugae, on the angulus and in the antrum, near and at the edge of the ulcer. However, no definite coating effect covering the ulcer in toto was noted.

#### DISCUSSION

In the quest of an ideal antacid, various substances are being combined so as to produce mixtures which might have a high antacid effect. One of such preparations was a mixture of aluminum hydroxide and magnesium trisilicate. This mixture which was prepared in different ratios by various pharmaceutical laboratories is being used widely under different names in the treatment of peptic ulcer patients. In comparing the result of observations of these mixtures with those of the individual component substances, there is noted a definite tendency toward better acidity control, slightly better clinical response, and less tendency to untoward side effects.

#### SUMMARY

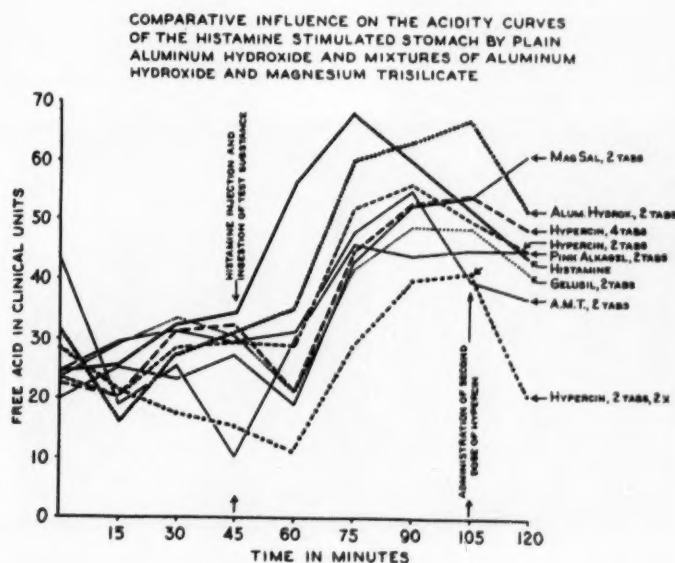
A study covering the observations on five antacids—Hypercin, Pink Alkajel, Gelusil, Mag-Sal, and AMT—containing mixtures of aluminum hydroxide and magnesium trisilicate is herewith reported.

The antacid study indicates that all of these substances had a better antacid effect than aluminum hydroxide alone.

While there were slight differences between these substances in their antacid effect, all of them significantly decreased the gastric acidity.

Four tablets of Hypercin had a slightly better antacid effect than two tablets. Two tablets given at hourly intervals had a very good and most prolonged antacid effect.

This study shows that all the substances tested had a marked antacid effect in peptic ulcer patients. The variations in the beneficial effects obtained clinically with some of these substances are probably due to factors other than purely decrease in acidity.



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## PRIMARY MEGACOLON IN YOUNG ADULTS

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THE FIRST description of megacolon was given by von Ammon (1842) over 100 years ago but little recognition was given the condition until Hirschsprung presented a paper on the subject in 1888. There have been numerous case reports since that time, but there have been relatively few large series of cases. The condition remains rare (1). Lewitan and his associates (2) quote Fenwick's observation of an incidence of congenital megacolon of one in 10,000 in a large series of necropsies performed in the London Hospital for Sick Children. The disease is even rarer in adults. Hiatt (3) reports only four cases over a five year period. Only 27% of Whitehouse and Kernohan's (4) patients with megacolon were over the age of 20 years. Hurst's (6) report included 26 patients over the age of 20 years, with most, if not all, of them falling under Lee and Bebb's (7) classification of "functional megacolon."

The present series consists of 11 young adults with primary megacolon. Ten of these were newly-inducted airmen in the United States Air Force and the eleventh is a military dependent.

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## CASE REPORTS

*Case No. 1:* This poorly developed somewhat poorly nourished 17 year old white male complained of cramping abdominal pains, one bowel movement per week and episodes of watery diarrhea all since the age of four years. He also complained of palpitation and had symptoms of hyperventilation. A slightly distended tympanitic abdomen was found on physical examination. Rectal examination demonstrated a large rectum, and this was further confirmed by sigmoidoscopy. The subphrenic radiolucency of the chest x-ray (Fig. 1) was suggestive of megacolon. A barium enema study (Fig. 1) revealed great dilatation of the entire colon and rectal ampulla down to the anal canal. The patient was started on urecholine, five milligrams orally three times a day and started having daily bowel movements.

*Case No. 2:* This patient was a well developed, well nourished 19 year old white male. At the age of 11 years, he developed abdominal pain, was diagnosed as having "too much intestine" and was subjected to surgery; and 18 inches of colon were removed. He continued experiencing flatulence, abdominal distensions, dizziness and occasional episodes of vomiting. At age 12 a temporary cecostomy was performed. At ages 13 and 15, laparotomies were performed because of "adhesions." His bowel habits have been regular, with one bowel movement per day, since the age of 11 years. The barium enema study (Fig. 2) demonstrated megacolon and megaileum. Equivocal results were obtained from trials with prostigmine, urecholine, mecholyl and tetraethyl ammonium chloride.

*Case No. 3:* This well developed, well nourished 19 year old white male had experienced constipation all of his life, manifested by bowel movements every six to eight days. Digi-

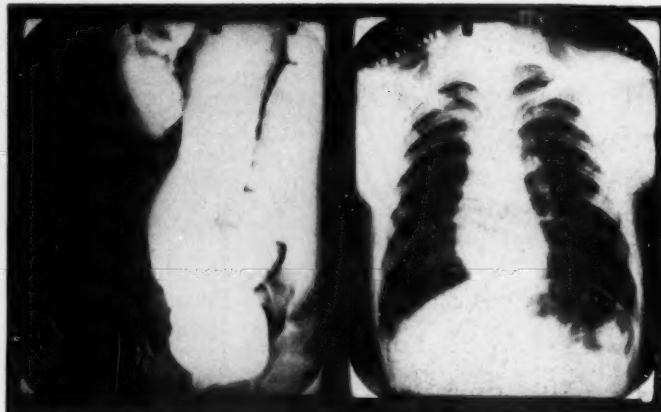


Figure 1



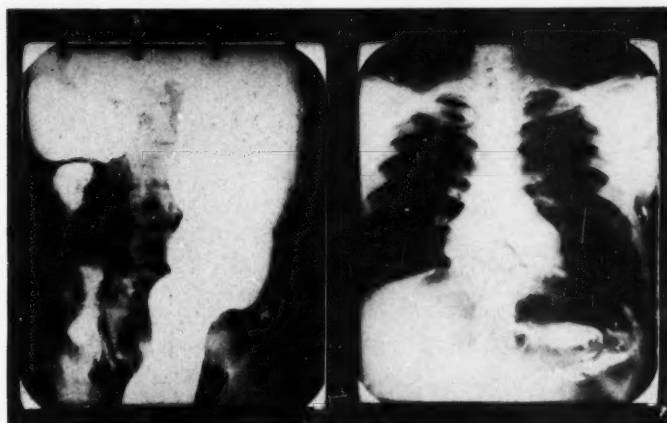


Figure 2

tal rectal examination and sigmoidoscopy revealed a widely dilated rectal ampulla and sigmoid colon. Megacolon was demonstrated by barium enema studies.

*Case No. 4:* This fairly well developed, fairly well nourished 26 year old white female had experienced severe constipation since infancy. Ordinarily she had bowel movements every three to six weeks, but on occasions the interval would be as long as three months. She admitted to no other complaints but had frequent episodes of fecal impaction, particularly since the age of 13 years and more particularly during the six months prior to her admission to this hospital. No medications had afforded her any appreciable degree of relief. Her family physician had tried a continuous caudal anesthetic for 48 hours on one occasion, but this afforded her no improvement. During the last trimester of each of her three pregnancies, she experienced bowel movements every two days. The large, tender colon was easily palpable on physical examination. The marked dilatation of the colon

was confirmed by a barium enema study. After prolonged medical management had failed to alleviate her symptoms, she was subjected to subtotal colectomy and four and one-half feet of the distal colon removed. Histologic examination of the excised segment of colon revealed normally appearing myenteric plexuses. In a short post operative follow up the patient is having regular bowel movements.

*Case No. 5:* At the time of admission to this hospital, this well developed, well nourished 18 year old white male was entirely asymptomatic and was having a bowel movement every one or two days. He underwent a surgical operation at the age of four years because of the diagnosis of megacolon, and an "abdominal sympathectomy" was performed. X-ray studies at this hospital, including chest x-ray (Fig. 3), flat plate of the abdomen (Fig. 4) and barium enema demonstrated that megacolon had persisted in spite of the absence of symptoms.

*Case No. 6:* This well developed, well nourished 22 year

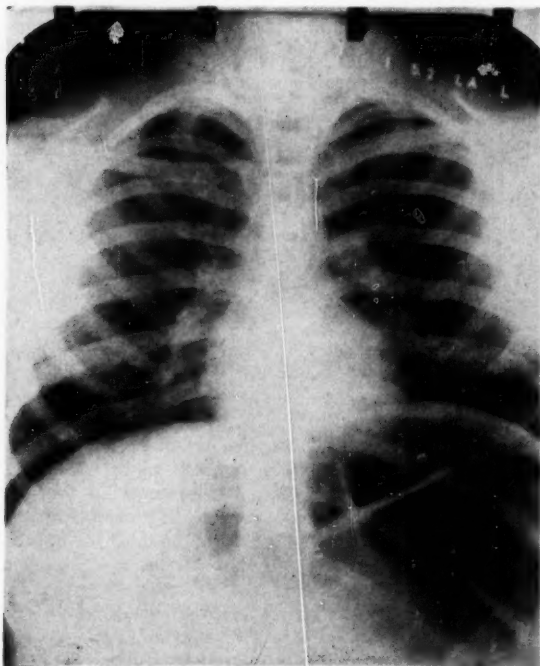


Figure 3



Figure 4

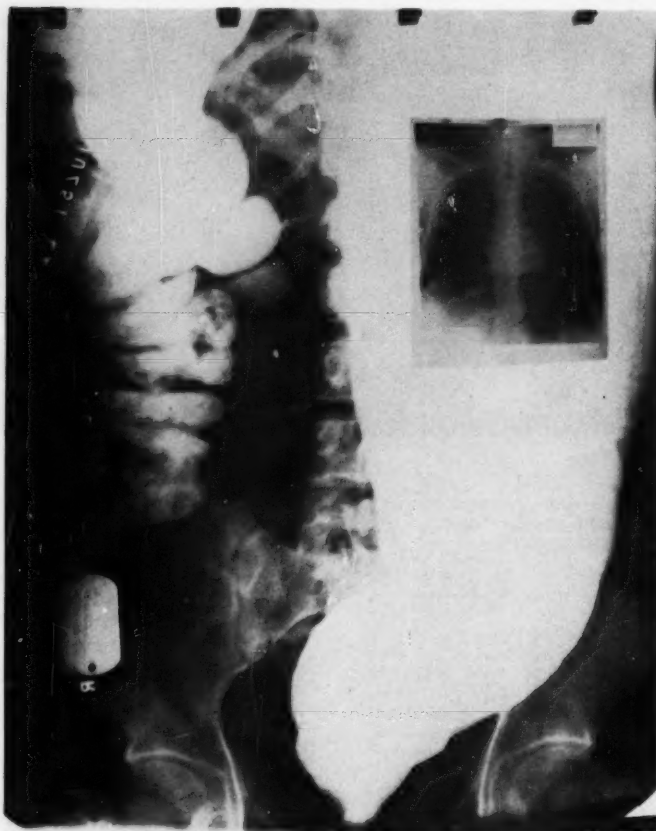


Figure 5

old white male was admitted for study because a routine x-ray of his chest (Fig. 5) strongly suggested the presence of megacolon. He admitted to an eight to ten year history of mild post prandial upper abdominal distension relieved by defecation. He never had noted persistent constipation and was having two bowel movements per day. Barium enema studies demonstrated marked dilatation of the entire left colon (Fig. 5).

*Case No. 7:* This well developed, well nourished 17 year old white male was placed under study because of a suggestion of megacolon noted on a routine chest x-ray. He was having a bowel movement every one to three days and was subject to occasional episodes of mild diarrhea. Barium enema revealed megacolon (Fig. 6).

*Case No. 8:* This well developed, well nourished 17 year old colored male was found to have a dilated colon on a routine chest x-ray (Fig. 7). He was entirely asymptomatic and observed a daily bowel movement; however, he did admit to the need of frequent enemas for constipation between the ages of seven and ten years. Tremendous dilatation of the sigmoid colon and rectal ampulla was noted (Fig. 7), with the bulk of the dilated colon being in the right side of the abdomen. The remainder of the colon was normal, but an interesting observation was the presence of a short segment of constriction (with a normal appearing mucosal pattern) proximal to the dilated segment.

*Case No. 9:* An x-ray study of the lumbar vertebrae of this well developed, well nourished 19 year old white male demonstrated prominent enlargement of the colon. He had absolutely no complaints referable to the gastrointestinal tract. A barium enema study confirmed the diagnosis of megacolon.

*Case No. 10:* This well developed, well nourished 24 year old white female was noted to have tremendous dilatation of

the colon on a routine chest x-ray (Fig. 8). She had no gastrointestinal complaints but did admit to mild constipation in childhood. Megacolon was confirmed by a barium study of the colon.

*Case No. 11:* During a routine physical examination of this well developed, well nourished 21 year old white male, palpation of the non-protuberant abdomen suggested the presence of large fecal masses. He admitted to mild constipation all of his life, but this had been appreciably reduced in adult life. The diagnosis of megacolon was established by barium enema studies (Fig. 9). An interesting variation in the appearance of this patient's colon was the presence of prominent haustral folds in the dilated colon.

#### DISCUSSION

Several different classifications of megacolon have been presented over the years. These have tended to be somewhat confusing because of the limited scope of some classifications, because of the failure to recognize many cases with mild symptoms, because of adherence to criteria which now are recognized to be too rigid, and because of the application of systems of therapy which were unphysiological. Regardless of the terminology employed, the essential factor is its application to a physiologic approach to therapy. When one encounters a patient with a dilated colon, a gross intrinsic or extrinsic block of the colon distal to the dilated segment must be sought (secondary megacolon). This is accomplished by the digital examination of the rectum, sigmoidoscopy and barium enema studies. The



Figure 6

absence of such a gross block indicates the disease to be primary megacolon. This type, too, is due to a block, even though it be of a functional nature. This may result from an aganglionic segment of colon, a pre-colonic neurologic defect or any of the other etiologies listed by Barger (8) or Bockus (9). Megacolon resulting from an aganglionic segment is usually characterized by a normal appearing segment of colon just proximal to the anal canal, and probably the only effective treatment is surgical removal of the aganglionic segment (10, 11, 12). This type of megacolon is more common in children, is more severe than the

other type of primary megacolon and probably is congenital in origin. The other general type of primary megacolon seemingly does not have an aganglionic segment, is milder in symptomatology, is the commoner type in adults and usually can be managed by a medical regimen. Contrary to earlier opinions, it is doubtful that the presence of megacolon in all these cases extends back to birth or even to infancy. Bockus (9) expresses doubt that all cases are due to a primary congenital defect. Cameron (13) expressed the opinion that an inflammatory neurological lesion might be responsible. de Natale (5) re-emphasized the possibility that megacolon can be acquired. Lewitan and his associates (2) reported 18 patients with megacolon found in the study of 120 neurological patients, most of whom had Parkinsonism. He considered his patients to have acquired the megacolon several years after the onset of the neurologic disease. Ishikawa (14) produced megacolon in dogs by sectioning the parasympathetic nerve supply to the colon. Adamson and Aird (15) produced megacolon in cats in similar experiments.

The patients in this series are all of the primary type (8). According to the classification of Lee and Bebb (7), all, with the possible exception of Case No. 2, would be classified as belonging to the functional type. Secondary megacolon was ruled out in all by digital examination of the rectum, sigmoidoscopy and barium enema studies. None of them showed a normal appearing segment of colon immediately proximal to the internal anal sphincter. With the exception of Case No. 4 fecal impaction was not a major factor in these patients. Interestingly, Case No. 4 did not benefit from a trial of spinal anesthesia. This agrees with the observations of Telford and Haxton (16) who reported that adults did not benefit from the procedure.

Bodian (17) reported on the familial incidence, and Stammers (18) has noted retardation of growth in patients with megacolon. In this series no familial incidence was observed and in only one patient did the question of retarded growth arise. It should be pointed out, however, that their observations probably are based on patients with the aganglionic type of megacolon. Leon and Karshner (10) have observed that spontaneous improvement in the symptomatology of megacolon may occur after adolescence. This was noted in five patients of the present series (Table I),



Figure 7

TABLE I

Patient	Age	Sex	Present Symptoms	Symptom changes since childhood	Suggestion of Megacolon on Chest x-ray
No. 1	17	M	Moderate	No change	Very suggestive
No. 2	19	M	Moderate	Improved*	Very suggestive
No. 3	19	M	Moderate	No change	None
No. 4	26	F	Severe	Worse	Suggestive
No. 5	18	M	None	Improved*	Very suggestive
No. 6	22	M	Minimal	Slightly worse	Very suggestive
No. 7	17	M	Minimal	No change	Suggestive
No. 8	17	M	None	Improved	Very suggestive
No. 9	19	M	None	No change	Suggestive
No. 10	24	F	None	Improved	Very suggestive
No. 11	21	M	Minimal	Improved	None

\*Surgical procedure prior to this analysis.

but two had undergone corrective surgery in childhood.

In the present series of patients with megacolon, one is impressed by the mildness of their symptoms. Only one patient was classified as severe, three were moderate, three were minimal and four had absolutely no

symptoms referable to the gastrointestinal tract (Table I). Only three of the 11 patients had the diagnosis of megacolon made prior to studies here. Diagnostic studies were initiated in five of the patients (not previously diagnosed as having megacolon) because of a suggestion of megacolon observed on a routine chest x-ray. One patient (Case No. 9) was noted to have a dilated colon when diagnostic x-ray films of the lumbar vertebrae were studied. Investigation was initiated in one patient (Case No. 11) after the clinician palpated a dilated, feces filled colon. The remaining patient (Case No. 3) was investigated because of a history of prolonged constipation.

This series of patients reemphasizes the value of the chest x-ray in the presumptive diagnosis of megacolon. This observation (6, 9) is not original in this series, but the present series beautifully illustrates the observation. The chest x-rays were suggestive of megacolon in nine of the 11 patients; and of these, six were strongly suggestive. The subphrenic areas of radiolucency, as exemplified by cases 5, 6, 8 and 10, could be due to few conditions other than megacolon. The chest x-ray of one of the patients (Case No. 8) exhibited a relative prominence of the subphrenic radiolucency on the right side instead of on the left side as is usual, however, this was explained by the barium enema which disclosed the presence of the dilated and elongated sigmoid colon in the right side of the abdomen. The chest x-ray of Case No. 10 demonstrated a shift of the heart to the right as a result of the markedly dilated colon. This has been noted previously by Hurst (6).

Prolonged follow up and long term evaluation of therapy were not feasible in this group of patients;

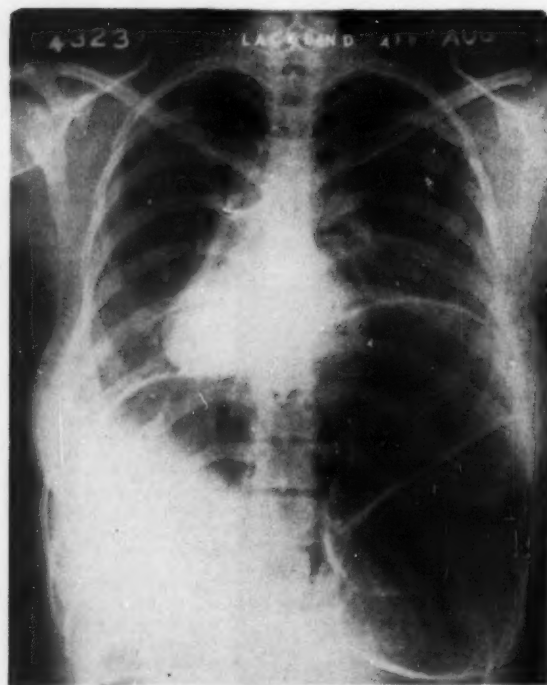


Figure 8



Figure 9



because all but one were in the military service and have been sent elsewhere.

#### SUMMARY

1. Eleven young adults with primary megacolon are reported. Nine were males, and two were females. Ten of them were white, and one was colored.

2. In this series of patients, the symptoms were impressively mild. Only three had the diagnosis of megacolon made prior to studies carried out here. Seven of the 11 patients had minimal or no symptoms referable to the gastrointestinal tract.

3. The suggestion of megacolon noted on routine chest x-rays was particularly valuable in the accumulation of this series of patients. Diagnostic studies were initiated on the basis of the chest x-ray in five of the patients.

4. One patient was presumed to have megacolon as the result of the observation of a dilated colon on x-ray films made in the study of the lumbar vertebrae. One patient was suspected of having megacolon when large fecal masses were palpated during a routine physical examination.

5. Pertinent literature is reviewed and applied to various interesting aspects of megacolon which were observed in this series of patients.

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## AN ANALYSIS OF INSULIN (HYPOGLYCEMIC) REACTIONS IN DIABETIC PATIENTS

### I. STATISTICAL SURVEY OF 203 CASES

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WE WERE led to undertake a study of insulin reactions because we were impressed by the frequency of their occurrence in patients consulting us for the treatment of diabetes. Further impetus was lent by the observation of permanent brain damage in a significant number of cases, and even death in one instance. If a satisfactory analysis of the contributing factors could be made, then application of this knowledge would be of value in improving diabetic management.

#### METHOD

An analysis was made of the case histories of 203 consecutive diabetic patients who were taking insulin when first encountered by one of us (J. I. G.). These were seen at two hospitals for chronically ill patients (27 cases), a Veterans Administration Hospital (114 cases) and private practice (62 cases). The group presented a mean age of 53 years with a distribution from the 2nd to 9th decades (Fig. 1).

JANUARY, 1954

Each patient was questioned carefully concerning the occurrence of insulin reactions at any time since the onset of the disease. The reactions were tabulated according to their character, severity, time of day and type of insulin in use. The final proof of the true nature of the reactions was based upon the clear-cut subjective response to the administration of carbohydrate, the temporal relation to the use of insulin or the demonstration of a low blood sugar when feasible. Cases in which there was reasonable doubt of the existence of an insulin reaction were eliminated. No attempt was made to ascertain the total number of reactions in any one patient. However, a separate entry was made in those patients who had experienced reactions on more than one type of insulin so that the frequency of this untoward effect with the various insulin types might be compared.

For the purposes of this paper the insulin reactions were separated into the mild and severe types. In the latter group were placed those patients in whom ob-

### AGE DISTRIBUTION OF GROUP STUDIED AND OCCURRENCE OF REACTIONS BY AGE GROUPS

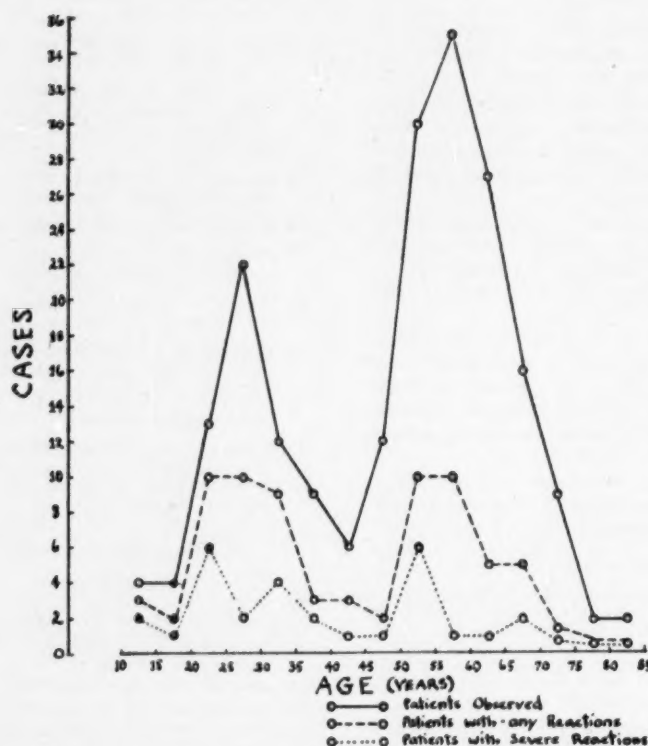


Figure 1

jective evidence of severe or lasting central nervous system or vascular damage was demonstrable. This included coma, convulsions, encephalopathy, hallucinations, personality changes, arterial thromboses and death. The cases presenting underlying vascular disease were reviewed critically and eliminated unless a specific relationship to hypoglycemia was clearly shown. Other cerebral symptoms of more transient nature such as dizziness, irritability, staggering, amnesia, confusion, etc., were classified as mild reactions.

#### RESULTS

Of 203 diabetic patients in this study, 77 (38%) gave a history of having had one or more insulin reactions at some time. The number of patients with reactions among 141 cases on the hospital services was 54 (38%) as compared with 23 (35%) among 62 private cases. It is seen that there is no significant difference between the figures for these two groups. Inasmuch as the proportionate use of the various insulin types and the age distribution are likewise similar, the two groups have been combined in the statistical data to be presented.

It is noteworthy that almost one-third of the entire group (62 out of 203), who had been taking insulin when first observed, were subsequently controlled on diet alone. Needless to say the great majority of these patients were overweight and soon became aglycosuric following institution of a weight reduction regime. Fourteen of these patients (22%) had had insulin re-

actions in the past. By contrast, the incidence of reactions was twice as high (45%) in the remaining 141 patients, who continued to require insulin. This emphasizes the well established fact that the obese diabetic who responds to diet alone is relatively insulin-insensitive. This is further borne out by the complete absence of severe reactions (as defined above) in these 62 patients as against 31 who had had such reactions in the remaining 141.

The seven insulin preparations most commonly used by patients in this group are presented in Figure 2 in order of decreasing frequency of use shown by the clear bars. The number of patients who had ever experienced reactions to each type of insulin is depicted by the striped portion of the bar. It should be pointed out again that these data are no indication of the actual incidence of reactions to any given insulin since neither duration of use nor the total number of reactions for any one patient are considered. Reliable information on these points is not available. Rather, this graph represents the ratio between the number of patients who employed this insulin and the number in whom reactions occurred. Since each of the seven preparations is considered in the same manner the method should provide a fair basis for comparison nonetheless. As one might anticipate, the most commonly employed insulins are regular and protamine zinc. Still, the recent tendency to the more frequent use of the intermediate insulins is apparent, thus providing means for their evaluation in this problem.

## INCIDENCE OF PATIENTS REPORTING REACTIONS WITH INSULIN TYPES

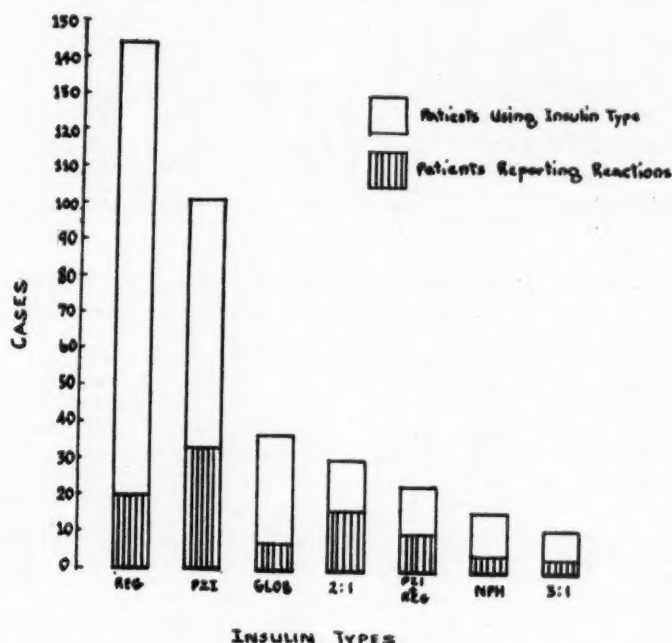


Figure 2

The occurrence of reactions among patients employing the various insulin types is also depicted in Figure 3. Regular insulin had been used at some time

## OCCURRENCE OF INSULIN REACTIONS

Insulin Types	No. Patients Using	No. With Reactions	Pct.
Regular	144	20	14%
Protamine Group	228	76	33%
a. PZI	102	33	32%
b. 2:1	30	16	33%
c. PZI + Reg.	23	10	43%
d. NPH	16	4	25%
e. 3:1	12	3	25%
f. All Others	45	10	22%
Globin	37	7	19%

Figure 3

during the course of the diabetes by 144 patients and produced hypoglycemic reactions in 20, an incidence of 14%. Protamine zinc insulin was used by 102 individuals and produced such reactions in 33 (32%), more than twice as often as regular insulin. When protamine zinc insulin had been combined with regular insulin, either as separate injections or in a 2:1 (regular:PZI) mixture, hypoglycemia was reported by 43% and 53%, respectively. Other mixtures with a smaller proportion of protamine (including NPH-50) produced a lesser incidence of reactions. Still, even these are seen to exceed the rate found with regular or globin insulin with zinc. It seems reasonable there-

fore to group together all the protamine mixtures and modifications for purposes of comparison. This is shown graphically in Figure 4 (a and b) in which the relative frequency with which patients used these insulins is compared with the relative frequency of reactions. Among the patients experiencing reactions, 74% had had reactions to the protamine group, 19% to regular insulin and 7% to globulin. The proportionate frequency of use of these insulins was 56%, 35% and 9%, respectively.

The incidence of severe hypoglycemic episodes (by the criteria defined above) is even more significant (Fig. 4c). Of the 203 patients in this study, 31 had had reactions of this type. Four of them had had severe insulin reactions on more than one insulin preparation which makes a total of 36 severe patient reactions. Twenty-nine of these (81%) were attributable to the protamine group. Only six severe reactions (16%) were encountered with the use of regular and globin insulin.\* The comparative frequency of use of the protamine and regular-globin groups was 56% and 44%, respectively. These data emphasize the role of the protamine group in producing severe hypoglycemia.

Further, it is of interest to compare the severe (labile) diabetic group with the mild group as regards the incidence of hypoglycemic reactions. This could be done most satisfactorily in the 62 private cases, with which one of us had had prolonged and intimate contact. There were 22 patients who were classified as severe, the remaining 40 being considered mild. Twelve

\*The type of insulin in use could not be obtained in one severe reaction.

### RELATIVE USE OF AND REACTIONS TO INSULIN TYPES

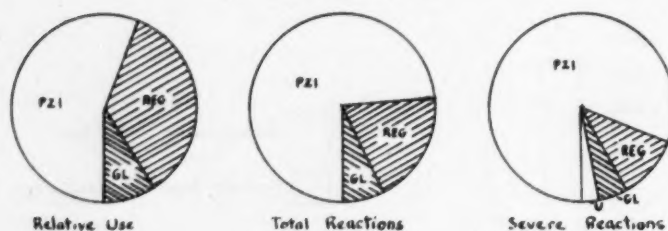


Figure 4

of the former (55%) gave histories of reactions as compared with 11 among the latter (27%).

The increased incidence of reactions among labile diabetics is, of course, not surprising. It may logically lead to another question as to whether the high incidence of reactions with the protamine group may not be due to the necessity for its more frequent use in controlling severe diabetes. However, our data fails to confirm this assumption indicating that the protamine insulins were actually employed less frequently here than in the mild group.

The patients with severe diabetes showed an increased tendency to reactions with *all* the insulin types employed. One can only conclude, therefore, that the increased susceptibility to insulin reactions is not associated particularly with the specific insulin in use, but is inherent in the nature of severe diabetes.

#### CONCLUSION

The data presented here indicate that the longer acting protamine zinc insulin and its various mixtures and modifications present greater potential hazards with respect to the occurrence of hypoglycemic reactions than the shorter acting regular and globin insulins. Not only is the higher incidence of these untoward

reactions shown, but a definite tendency to more severe reactions and irreversible, organic brain damage is also predominant with the protamine group. This is not to imply that there is no place for these insulins in the management of diabetics, but simply that greater caution and understanding is necessary for their proper use. This subject is discussed more thoroughly in a subsequent paper.

#### SUMMARY

In a series of 203 diabetic patients using insulin, 77 (38%) had had at least one hypoglycemic reaction. Of the group, 62 were subsequently controlled by diet alone and these had a lower incidence of reactions (22%) than did the remaining 141 (45%). Regular insulin was most commonly used and produced reactions in 14% of its users. Protamine zinc insulin, when used alone, or as a mixture and modification gave reactions in 33%. Of the severe reactions in the group, 81% were attributable to the protamine group.

Fifty-five per cent of labile diabetics had had reactions in contrast to 27% in mild diabetics. It is concluded that the protamine group presents a greater potential hazard as regards the incidence and severity of insulin reactions than regular and globin insulin.

## INTUSSUSCEPTION IN ADULTS DUE TO DIVERSE TUMORS OR SIMILAR STRUCTURES

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THE FOLLOWING is a series of six cases of intussusception in adults collected during the 1948-52 period, caused by diverse tumors or similar structures (that is, their mechanism of production has been the same, although not all have been strictly neoplasms), and placed in different segments of the intestines. Three of them have been enteric (ileo-ileal), two ileo-cecal and one colic (ceco-colo-rectal). Three were due to benign tumors, one was caused by aberrant pancreatic tissue in the ileum, one by Meckel's diverticulum with four ascarides inside and only one was a malignant tumor (myosarcoma of the ileum). We have tried to summarize them in Table I.

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Submitted May 21, 1953.

#### PRESENTATION OF CASES

*Case 1.* J. B. B., a man, 23 years old. Appendectomy 6 months previously. Two days before examination, had colicky pains, diarrhea and tenesmus. Vomited the first time the morning he was examined. Physical examination revealed a thin, pale young man, in great pain. The abdomen was not distended and a hard, long, movable and painful mass, about 4 inches long, could be felt in the right lower quadrant. No borborygmus. Patient's axillary temperature was 98.6°F, rectal temperature 99.5°F, pulse rate 80 and blood pressure 120/80. A tentative diagnosis of hypertrophic intestinal tuberculosis was made. He was interned and observed at frequent intervals.

Next day, the mass was smaller. He passed no gases and no evacuations. He refused intubation. On the third day, temperature was normal, pulse rate 108, abdomen moderately distended and borborygmi and slight gurgling noises could be heard. Neither fecal matter nor gases were passed. At 5 p.m., he complained of colicky pains and vomiting. Pulse rate was 124, and his abdomen was distended, with consider-



TABLE I

Case	Age	Sex	Preoperative diagnosis	Type of intussusception	Operated	Variety of tumor	Immediate results
1	23	m	Obstruction small bowel	Ileo-cecal	yes	Myosarcoma ileum	Recovered
2	16	f	Intussusception. Gall-stone ileus?	Ileo-ileal	yes	Polyposis of small intestine	Recovered
3	44	f	Sigmoid rectal Intussusception	Ceco-colo-rectal	yes	Lipoma of cecum	Recovered
4	38	m	Intussusception	Ileo-cecal	yes	Lipoma of s. bowel	Recovered
5	14	f	Tuberculous peritonitis	Ileo-ileal	no	Aberrant pancreas	Died
6	17	m	Appendicitis Peritonitis	Ileo-ileal	yes	Meckel's diverticulum Ascariides	Died

able increase of borborygmi and gurgling noises. He was operated on at 7:45 p.m., under the diagnosis of obstruction of the small bowel. An ileo-cecal intussusception appeared. The small intestine was distended and hyperemic. In the ileo-cecal region, about 15 cms. from the cecum, a rounded mass was seen and felt. The loop was infarcted, so 30 cms. of gut was resected and an end-to-end anastomosis performed, rather close to the ileo-cecal valve. Suction was maintained by means of an in-lying Miller-Abbott tube. Postoperatively, the course was uneventful for the first two days. Pneumonia and diarrhea appeared on the third day. That night he had 12 intestinal evacuations. With penicillin, sulfaguanidine and emetine he recovered rapidly. Histological examination of the excised gut revealed a myosarcoma of the ileum with superficial necrosis (See Fig. 1). Immediate results were good. Examined periodically. Roentgenological examination was normal. However, we have lost track of him lately.

Case 2. D. F. C., a 16 year old girl, suffered for the last three years from epigastric pains, specially after the ingestion

of fats and without apparent acute crises. Normal menses. On the previous day, and as a result of eating alligator pears (avocados), she had colicky abdominal (periumbilical and epigastric) pains, with distension, nausea and vomiting. Constipated for the last three days, had passed no gases since the day before. She consulted because her pains became more acute. When examined, she was pale, dehydrated and in great pain. Axillary temperature was 97.5°F, rectal temperature 100.4°F, pulse rate 120 and blood pressure 105/80. The abdomen was distended, with muscular defense on the left lower quadrant and tympanic on percussion. Blumberg's sign was positive and the whole abdomen was painful as well as both costo-lumbar regions. Gynecological examination disclosed tenderness of the left and posterior vaginal walls. Examination of corpus uteri and adnexa was not satisfactory because of muscular tension. A tentative



Fig. 1: Myosarcoma of the ileum. Photomicrograph with a magnification of 180 diameters, showing atypical cells and rests of intestinal glands.

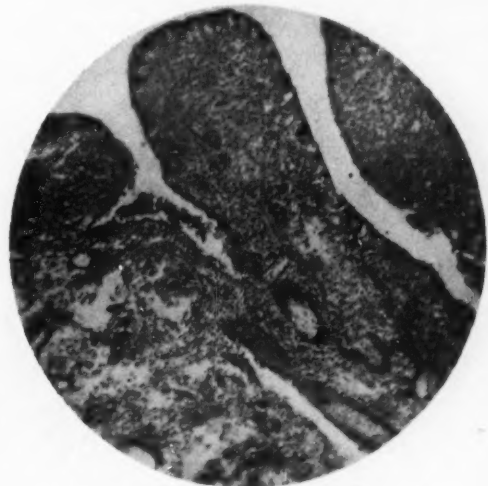


Fig. 2: Polyposis of the small intestine. Photomicrograph showing protruding submucous tissue uplifting the mucous membrane and covered by debris of glandular fundi in the middle of a necrotized mass formed by leukocytes, edema and necrotic hemorrhagic infiltration.

diagnosis of acute pancreatitis and cholelithiasis was made and she was left under observation.

Four hours later, after a large enema, she not only passed abundant feces but also a certain amount of blood (melena). Although her general condition remained the same, both pain and vomiting had stopped. Rectal digital examination disclosed discrete pain in the cul-de-sac of Douglas. Red blood cells numbered 3,480,000, white blood cells 12,200, neutrophils 92 per cent, monocytes 3 per cent, lymphocytes 3 per cent. Hemoglobin was 70 percent. Hematocrit 30.3 per cent.

Two hours later, she was restless and pale. She vomited, passed no gases and suffered from tenesmus. Abdomen was tense, painful and tympanic with marked defense and borborygmi. Colicky pains came at frequent intervals. With the provisional diagnoses of intussusception or gallstone ileus, she was immediately operated on. When the abdomen was opened, enteric intussusception (ileo-ileal) was observed. On decompression, 40 cms. of ileal necrosis was found and a necrotic polyp, probably the cause of intussusception, inside the loop. Intestinal resection of 1.20 mt. was performed followed by end-to-end anastomosis. Microscopical examination of resected segment showed multiple polyposis of the small intestine. Necrotic polyps varied in size from that of a small lentil up to 6 cms. (See Fig. 2). Recovery was uneventful and she was sent home in good condition.

*Case 3.* G. V. L., a 44 year old woman, had been admitted to a hospital in July 1950, suffering from dysenteric disorders. Although released, she continued with abdominal pains, cramps, belching, vomiting and occasional diarrhea.

Two months later, on September 1, she suddenly complained of tenesmus, colicky pains, vomiting, dysuria and rectal hemorrhage. Her condition became gradually worse, until she consulted five days later (Sept. 6). When examined, she appeared thin, dehydrated, anguished and in considerable pain. Axillary temperature was 98°F, pulse rate 120 and blood pressure 120/100. Marked periumbilical pain. Abundant fetid bloody rectal secretion was observed on inspection of the anal area. On rectal digital examination, the sphincter was found hypotonic. Two centimeters from it, a soft, smooth mass was felt, about the size of a fist, easily followed by the finger, except to its upper limit. There was an intestinal orifice in its center that on proctoscopic examination was seen to be a prolapse of the sigmoid loop into the rectum, showing a dark red hue. Colic intussusception was diagnosed and the patient was prepared for operation. Red blood cells were 3,750,000, white blood cells 11,200, neutrophils 91 per cent, monocytes 5 per cent and lymphocytes 4 per cent.

Once the abdomen was opened, no cecum could be visual-

ized. Both the colon's transverse and descending segments were distended and an intussuscepted intestinal loop could be felt inside. After painstaking decompression, a large cecum was observed with a soft, smooth tumor in it, about 6 cms. in diameter. There were also mesenteric and mesocolic hypertrophied glands. Judging it as malignancy of the cecum, the acting surgeon performed a right hemicolectomy up to the middle of the transverse colon, followed by side-to-side entero-anastomosis (ileo-transversostomy).

On microscopical examination, the tumor turned out to be a submucous lipoma of the cecum, about the size of an egg. Surrounded by a thin capsule it was of a yellowish color and crossed by a great number of thin vessels. On histological examination, the capsule was proved to be cecal mucosa and the yellow mass, adipose tissue (See Fig. 3). Examination of the glands, merely showed discrete hyperplastic lymphadenitis. Postoperative course was followed by complete recovery. Control roentgenological study, performed weeks later, was normal.

*Case 4.* A. P. J., a 38 year old man without previous digestive disorders. On June 3, 1951, half an hour after breakfast he suffered acute diffuse abdominal pains, afterwards localized in the periumbilical area, together with vomiting noncharacteristic in quality, and belching. Five hours later, his symptoms became worse and he sought medical advice. Pale, lucid but restless and plaintive, his axillary temperature was 97.5°F, his pulse rate 100 and blood pressure 160/90. His tongue was moist, but slightly coated. Abdominal examination evinced discrete distension of the right flank and quadrant. In the latter, a soft, diffuse, rather tender mass of from 4 to 8 cms. in diameter could be felt. At certain moments it became harder and more painful. Intussusception was diagnosed and the operation was immediately performed.

On opening the abdomen, a great movable cecal tumor was observed. On closer examination, it turned out to be intussusception of the ileum into the cecum. Decompression was difficult. Once accomplished, a considerable portion of the small intestine presented marked necrosis. Ninety centimeters were resected, starting from the ileo-cecal valve, followed by side-to-side entero-anastomosis (ileo-transversostomy).

Microscopical examination showed this tumor to be a pedunculated ileal lipoma (See Fig. 4). The patient recovered completely.

*Case 5.* S. J. C., a 14 year old girl was sent to our hospital from Santa Cruz after treatment there for 10 days. On July 11, 1951, she complained of asthenia, weakness, fever, thirst, loss of weight, coughing, persistent abdominal pains,

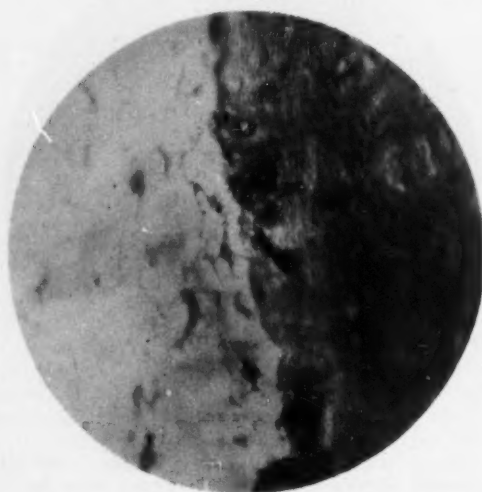


Fig. 3: Lipoma of the cecum. Photomicrograph showing to the left fat tissue and to the right the mucous membrane covering it.



Fig. 4: Lipoma of the ileum. Fat tissue on the left covered by the ileum's mucous membrane, on the right. Photomicrograph with a magnification of 180 diameters. Hematoxylineosine dye.

anorexia and constipation. Admitted at the local hospital, as her condition did not improve, she was sent to ours, where the resident surgeon on duty examined her and diagnosed miliary and peritoneal tuberculosis. Three days later, she was transferred to our department. Physical examination then revealed her as a pale, querulous, conscious girl, without fever, but her general condition was very poor, with a pulse rate of 90 and a blood pressure of 110/70. The tongue appeared dry and coated and her distended abdomen, easily depressed and painless on palpation, evinced shifting dullness on percussion of the hypogastric region. The consulting gynecologist esteemed the adnexa to be enlarged and advanced a provisional diagnosis of genital tuberculosis, not confirmed later. On that day she passed normal stools, a fact worth remembering. Blood examination revealed non-protein nitrogen 37 mg. per hundred cubic centimeters, sedimentation rate 30 mm. per hour, red blood cells 4,300,000, white blood cells 12,700, neutrophils 73 per cent and lymphocytes 24.5 per cent. Hemoglobin was 13.3 g. Roentgenological examination of the chest was normal, but "fluid levels" were observed on surveying the abdomen.

Next day, in spite of intense fluid and mineral therapy, she still appeared dehydrated. The abdomen was still more distended and rather painful in the hypogastric region. Although that day she passed no stools, she did so the next one (sixth day of admittance and third in our own department), passing once more normal stools, a fact we wish to stress again. Her condition remained unchanged on the following one, seventh day in hospital. That night, she died suddenly. She was never feverish and her pulse rate always fluctuated between 80 and 90. Post mortem examination disclosed an enteric intussusception (ileo-ileal), about 12 cms. long, with marked necrosis of the bowel walls. In the site of intussusception, where the ileum was, a soft nodule of the small bowel protruded beneath the mucosa, about one centimeter in diameter, of a dark red hue. On microscopical examination, it presented a glandular structure divided into lobules and in their center, islets of Langerhans with small excretory ducts appeared. In short, it was a nodule of aberrant pancreatic tissue (See Fig. 5).

*Case 6.* F. M. S., a 17 year old youth had been healthy until the day before, when after excessive eating and drinking, he suddenly complained of headache, vomiting, diffuse colicky abdominal pains, malaise and diarrhea. His physical condition was extremely poor and he was not quite lucid. Axillary temperature was 102.2°F, rectal temperature 103.6°F, pulse rate 124 and blood pressure 130/70. The tongue and lips were dry, the former coated. His abdomen was distended and tender in both iliac and hypogastric regions. When first

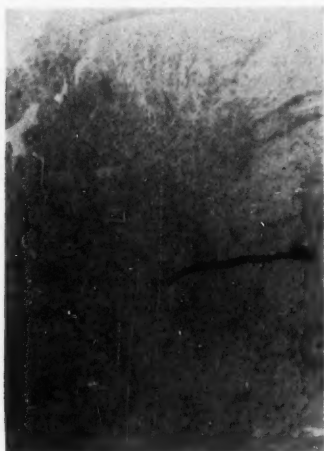


Fig. 5: Aberrant pancreatic tissue. Photomicrograph of the ileum's nodule. On the left, intestinal membrane and on the right, pancreatic glandular tissue. Hematoxylin-eosine dye X 180.

examined, a provisional diagnosis of acute toxic gastroenteritis was made, leaving him under close and frequent observation and with the usual treatment. That night he vomited continually. Next day, he was feverish (temp. 100°F), his tongue was dry, the abdomen was still distended and on rectal digital examination, cul-de-sacs were painful. Blood examination disclosed 5,380,000 red blood cells, 7,200 white blood cells, neutrophils 84 per cent, monocytes 6 per cent and lymphocytes 10 per cent.

With a tentative diagnosis of appendicitis and peritonitis, he was operated on at once. When the peritoneum was opened abundant seropurulent fetid secretion flowed. The small bowel loops appeared red and distended. A retrograde and thickened appendix was removed. At about 20 cms. from the ileo-cecal valve, an enteric intussusception (ileo-ileal) could be seen and 5 cms. from it, the bowel was perforated allowing its contents to pass into the peritoneal cavity. It was about to perforate in many other places. Decompression was unsuccessful, so 50 cms. of bowel were resected, including intussusception, perforation and near parts about to perforate. End-to-end anastomosis. The patient left the operating room in a very critical condition. Pulse rate was 120 and blood pressure 90/50. Although every precaution was taken, (two liters of plasma were infused during operation and he received proper stimulants), he died that evening at 8:30 p.m. On histological examination, the intussuscepted segment showed marked necrosis and on being opened, it disclosed a five centimeter long Meckel's diverticulum (see Fig. 6) and four ascarides into its pouch. No anatomical sign of typhoid fever was found.

#### DISCUSSION

A perusal of current medical literature (1), might incline one to believe that tumors often cause intussusception. This deduction is justified if large series collected by different authors (2) are analyzed. However, in general practice, intussusception in adults seems to be uncommon. The central districts of our city have 600,000 inhabitants and all the acute cases, both medical and surgical, are treated at the Asistencia Publica. The San Miguel district, where the Barros Luco hospital lies, has 140,000 inhabitants. The total of patients attended during the 1948-52 period, both at the Asistencia Publica and the Barros Luco Hospital, where our patients were observed, and the number of intestinal obstructions and intussusceptions in the adult, are presented in Table 2.

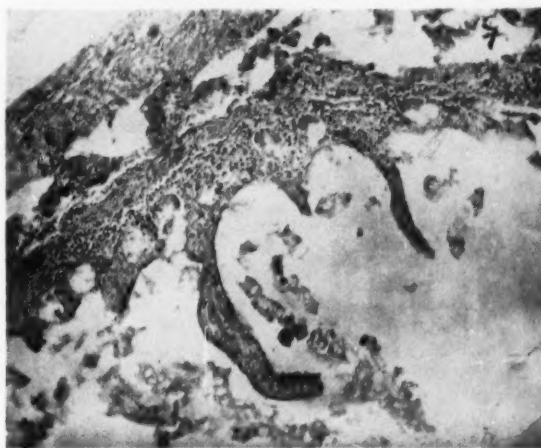


Fig. 6: Meckel's diverticulum. This photomicrograph shows the walls of Meckel's diverticulum with areas of edema, necrosis and inflammatory and hemorrhagic recent infiltration.



TABLE II

Asistencia Publica		Intest. obstructions	Intussusceptions
Year	Number of cases		
1948	188,858	27	2
1949	189,693	36	3
1950	200,130	25	1
1951	205,215	33	5
1952	202,944	26	1
	986,840	147	12
Barros Luco Hospital (Emergency ward)			
1948	no data	21	1
1949	1,520	14	—
1950	1,563	11	1
1951	2,379	10	—
1952	2,820	26	2
		82	4

Out of this total of 16 cases of intussusception (12 from the Asistencia Publica and 4 from the Barros Luco Hospital), only 8 were caused by tumors, including the case of Meckel's diverticulum (7 from the A. Publica and 1 from the Hospital). As can be seen, the total number of intussusceptions observed in the adult is not large, although, proportionally, a good

number of them is produced by tumors. We consider our series unusual and worth reporting because of the variety of tumors and their diverse localization. It is generally accepted (1) that lipomas (cases 3 and 4) and Meckel's diverticulum (case 6) are common causes of intussusception. Multiple polyposis occurs more frequently in the colon (Bockus). That multiple polyposis of the small intestine (case 2) can produce invagination has been mentioned by Horsley and Kearby (3), but sarcoma of the ileum (case 1) as cause of intussusception is distinctly rare and aberrant pancreatic tissue (case 5) is so unusual a cause, that Wangenstein (1a) does not mention it in his monograph.

## SUMMARY

A series of six cases of diverse tumors and embryogenic tissues as cause of intussusception in the adult is presented and their frequency is discussed.

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## LEIOMYOSARCOMA OF THE STOMACH: A CASE REPORT

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**L** EIOMYOSARCOMA of the stomach is a rare gastric lesion amounting to 1 percent of gastric tumors (17). The correct diagnosis is unusual but preoperative suspicion is increasing with the use of the gastroscope. Leiomyosarcoma of the stomach may simulate either benign or malignant gastric tumors. Its differentiation at times is difficult. In 1945 Paul reported a case of neurofibroma of the stomach which was strikingly similar in gross appearance to the gastric leiomyosarcoma discovered in the case we are reporting here (1).

The purpose of this paper is to emphasize the similarity in appearance of gastric polypi and stress the importance of surgical removal and microscopic study as the only means of establishing the benign or malignant nature of the lesion.

## REVIEW OF THE LITERATURE

Gastric sarcomas have been classified by Ewing into 3 histological groups: leiomyosarcoma, lymphosarcoma and round cell or alveolar sarcoma (17). Microscopically the leiomyosarcoma is made up of immature muscle cells, varying in degrees of differentiation. These muscle cells are grouped into bundles and bands by fibrous stroma. Active mitosis establishes the malignant nature of this lesion (18).

Gastric leiomyosarcomas have been classified ana-

tomically into 2 further types, the endogastric and the exogastric (7, 13). The endogastric lesion is situated in the submucosal surface and usually is encapsulated. It involves the mucosa secondarily by producing a central area of ulceration. The gross appearance of this ulcerated area in the polypoid mass resembles the uterine cervix. Ulceration may occur in any expanding endogastric tumor.

Endogastric leiomyosarcomas are reported to range from 1 centimeter to more than 10 centimeters in diameter. They may be sessile or pedunculated (7). Grossly the tumors are rubbery and compressible whereas carcinoma is hard and infiltrative (7). Central necrosis of this tumor is common and bouts of fever may mark the clinical course (5, 6, 7). The mucosa covering this lesion appears almost normal except for the central area of ulceration and the stretched out pattern of the rugal folds.

The exogastric type of leiomyosarcoma is reported to be one of the largest tumors encountered in the stomach (7, 10). The subserosal layer is primarily involved and the surrounding viscera are damaged by compression rather than by invasion (10, 11).

Leiomyosarcomas tend to arise from the greater or lesser curvature and are rarely encountered in the pylorus or cardia (3, 10, 14). These gastric lesions have a low degree of malignancy but occasionally a small tumor may give rise to widespread metastasis

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(11). The reported cases have had a very small incidence of metastasis at operation but a recurrence in the liver within 2 to 4 years has occurred frequently (14). Infiltration of the stomach wall itself is usually not extensive (14).

The gastroscopic examination frequently establishes the presence of a gastric polyp but the differentiation from a benign gastric lesion is not possible by this procedure. The tumor appears as a mass of varying size, protruding into the lumen of the stomach when visualized through the gastroscope. The mucosal folds surrounding the lesion may have a stretched appearance as they approach the surface of the tumor (10). This has been called the "phenomenon of bridging folds," and usually suggests that the tumor is of submucosal origin (10). The space between the surface of the tumor and the surrounding mucosa when bridged by stretched mucosa is a significant gastroscopic finding in gastric polyps (10).

The symptoms produced by gastric leiomyosarcoma vary from vague abdominal distress to pain simulating that of peptic ulcer (5, 6, 7, 8, 13). Occasionally the pain responds to medical management. Bouts of hematemesis and melena associated with superficial ulceration occur as the lesion progresses. Severe acute bleeding may occur at times but slow chronic blood loss is more frequent (7). When the tumor is exogastric, an abdominal mass may be felt (7). X-ray evidence of a filling defect showing a mucosal niche is frequently

demonstrated (15, 16). There is no relationship between anacidity or hyperacidity and the occurrence of gastric leiomyosarcoma (7).

The differential diagnosis includes lymphosarcoma, which is an infiltrating type of tumor and requires x-ray therapy rather than surgical intervention (2, 7, 10, 15). Carcinomas of the stomach are far more rapid in their course and usually the patient is more cachectic. Grossly the differentiation of malignant from benign lesions is impossible at times even with combined use of the gastroscope, gastro-intestinal x-rays and the examination of the gross surgical specimen.

Treatment for leiomyosarcomas of the stomach is surgical resection. The lesion is radioresistant in contrast to gastric lymphosarcoma (2, 7, 11).

#### CASE REPORT

G. F. was admitted to the University Hospitals on October 6, 1952. He was a 79 year old farmer who complained of epigastric pain which had occurred intermittently for 3 years. The pain increased in intensity and became persistent in type about 6 weeks prior to admission. He obtained moderate relief of his distress by ingestion of antacids and foods. No tar colored stools had been noted by the patient. He had recently lost 21 pounds.

The physical examination revealed an alert white man of 79 years who was not in any acute distress. There was little evidence of weight loss. Moderate tenderness was elicited on palpation of the epigastric area but no masses were felt. Laboratory examinations showed no occult blood in the stools. The hemoglobin was 12 grams, red blood count 5 million per cubic millimeter and the urinalysis was normal. A gastric



Neurofibroma of the stomach—case G. M.



Leiomyosarcoma of the stomach—case G. F.

analysis revealed no free acid but 5° of free acid was present after histamine. The gastro-intestinal x-ray studies showed a polypoid mass in the pars media with a central area of ulceration. A gastroscopic examination was performed. The scope was introduced with ease to the distal part of the pars media or depth I. The angulus was visualized and appeared normal in contour. The pyloric antrum and pylorus were poorly visualized but the mucosal surfaces that were observed did not appear unusual. About the median portion of the pars media or depth II, the mucosa was atrophic. Petechial hemorrhages, gross blood, numerous high lights, and sub-mucosal vessels were evident on the anterior wall of the lesser curvature. A polypoid lesion was seen on the lesser curvature about its median portion. It was viewed from the lateral aspect and visualization of the surface of the tumor was not possible. The mucosa surrounding the tumor was smooth and stretched out. There was no visible evidence of ulceration. The lesion was about 3 centimeters in diameter. The visualized portion of the posterior wall was normal. The crest of the cardia at depth III appeared normal. The impression was that the lesion represented a gastric polyp. Surgical excision was recommended. At the time of operation on November 3, 1952, a partial gastrectomy was performed. A mass was found on the median portion of the lesser curvature. Grossly the surgical specimen consisted of two thirds of the stomach wall which was distorted by a large soft nodule measuring 3.5 centimeters in diameter. The top of the nodule showed an area of ulceration 5 millimeters in diameter. On cut section the nodule appeared well encapsulated and consisted of grayish white hemorrhagic tissue. The rugae surrounding the lesion appeared stretched out as the mucosa ascended to the surface of the tumor. The stomach wall was not thickened and the serosal surfaces were not altered. The microscopic sections revealed the gastric mass to be composed of irregular bundles of smooth muscle fibers which were covered by a thin muscular coat and gastric epithelium. The nuclei of these bundles of muscle fibers showed pleomorphism. The sections of the ulcerated areas showed replacement of gastric epithelium by fibrinous exudate resting on chronically inflamed granulation tissue. The underlying submucosa showed marked fibrosis. The lesion did not appear to be invading the muscle coat of the stomach. The sections were interpreted as leiomyosarcoma of the stomach.

The post-operative course of the patient was uneventful. At the time of discharge from the hospital he was clinically improved and free of his previous symptoms.

#### SUMMARY AND CONCLUSIONS

Endogastric leiomyosarcomas are polypoid tumors that have a low degree of malignancy and arise from the greater or lesser curvature of the stomach. A central area of ulceration is frequently associated with this lesion, producing symptoms simulating a peptic ulcer or causing a secondary anemia subsequent to chronic bleeding.

A case of gastric leiomyosarcoma is reported. The gross specimen resembled the lesion found in the case of neurofibroma previously reported by Paul (1). The similarity of the lesions was so striking that these 2 cases were selected to illustrate the difficulty in differentiating malignant from benign gastric polypi by gastroscopic, roentgenologic and macroscopic examinations.

It has been found necessary to explore surgically all cases of gastric tumors for the prognosis of lesions

as leiomyosarcoma is improved by early surgical removal. Lymphosarcoma of the stomach produces a lesion similar in appearance and must be differentiated from leiomyosarcoma. Lymphosarcoma responds better to irradiation therapy; however, surgical exploration and biopsy are often necessary to establish the diagnosis of this tumor (2).

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## DUODENAL OBSTRUCTION AS REFLEX PHENOMENON DURING CHOLEDOCHUS STONE IMPACTION

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**O**BSTRUCTION OF the duodenum, like that of any duct or canal, may be classified as complete or partial. In complete obstruction or occlusion the passage is stopped altogether, while in partial obstruction or stenosis the progress may be retarded and the transit disturbed, though not completely blocked.

In the case presented here, there was a marked obstruction present at the third portion of the duodenum. While some of the barium passed through the narrowed lumen, the bulk was retained for many hours.

This obstruction, as demonstrated by x-ray, possessed all the earmarks of an organic stricture with corresponding dilatation of the proximal segments, although it proved to be a reflex phenomenon. It was demonstrable only during the painful period of a biliary colic, caused by the impaction of stone in the common duct. As soon as the attack was over, the obstruction in the transverse segment of the duodenum promptly disappeared.

This observation seems to be unique, inasmuch as no similar descriptions were found in the literature at my disposal. It, therefore, seems to be worthy of publication.

### REPORT OF A CASE

Mrs. T. D., white, female, 49, married, was first seen at my office in 1931. At that time she was suffering from ulcerative colitis of a few months duration. Her condition was considered fairly, though not excessively, severe. She responded

well to treatment. Recurrences developed in 1937 and in 1940. Roentgen examination revealed typical sausage shaped, un-hausted colon from the splenic flexure down to the rectum. Patient had no recurrences for the past twelve years. General condition and nutritional state remained satisfactory throughout.

Patient also suffered from gallbladder disease. The first severe biliary attack was diagnosed in 1928. In 1931, when first seen at my office, the gallbladder was of normal size, harboring one large non-calcium containing stone, as visualized by the Graham-Cole method. In 1937 x-ray of the gallbladder also revealed the presence of numerous smaller stones. In 1945 patient suffered from severe and often recurring gallstone attacks. By that time the gallbladder was enormously enlarged, harboring innumerable stones of varying size, some with calcium content and some without. Operation revealed a huge gallbladder, approximately two-fisted in size, with markedly thickened walls, showing signs of severe chronic inflammation. More than 100 stones were recovered, the majority of which were small, faceted, dark stones, with the larger ones having calcium layers. The largest stone, nearly nut-sized, was located in a huge diverticulum of the cystic duct, which, compressing the duct, produced *hydrops vesicae felleae* with the typical white bile. Patient stood the operation very well and was in good health thereafter, until the onset of the present ailment.

*April 1, 1953.* When patient called at my office, the first time for the present condition, the following history was given. Present ailment started six months ago. Patient suffered from very sharp and painful epigastric attacks, which she characterized as being practically identical with those choelithiatic attacks of the past. At the onset, they occurred once a month, gradually increasing in frequency until finally they appeared as often as twice a week. Each painful attack



Fig. 1A: Film taken in 1931. Gallbladder is of normal size and fair concentration power. It contains one negative stone shadow.

B: Film taken in 1945, just prior to surgery. Gallbladder is not visualized, even with double amount of dye (6 gm. priodax), indicative of poor functioning power. It contains 3 large gallstones, with some peripheral calcium deposit. They are far apart, indicating that the gallbladder must be of very huge size. The uppermost and largest stone was located in a huge diverticulum of the cystic duct (operation).

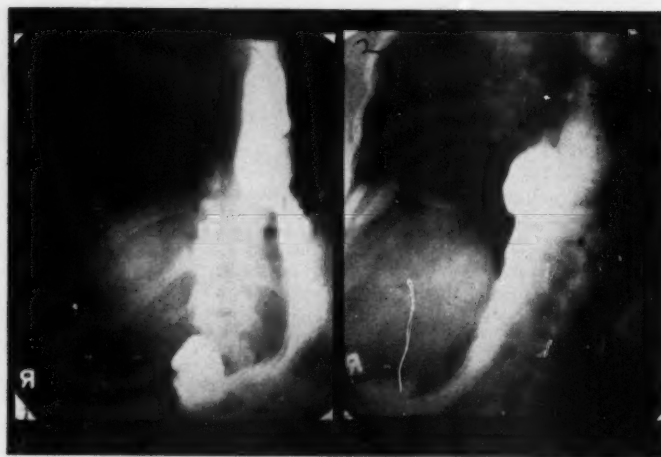


Fig. 2A: Cardiospasm. The esophagus is markedly though not excessively dilated.

B: Hiatus hernia. Protrusion of the stomach through the esophageal hiatus of the diaphragm. About one fourth of the stomach is thoracic.

lasted at least three or four hours and it did not seem to be correlated to food intake. Between attacks she felt perfectly well. She never had yellow jaundice, fever or chills. She lost about ten pounds during the present illness. In October, 1952, her local doctor arranged for an x-ray check-up to cover the gallbladder region, the site of the choledochus, the stomach, duodenum and small intestines. These examinations proved fully negative. Belladonna, demerol, local heat and diet had hardly any effect. Some of her physicians considered her a psychosomatic case, due to the fact that the patient worried considerably about her mother's having been afflicted with a possible carcinoma of the lung.

Physical examination was largely negative, except for some local tenderness at the epigastric region, and to the right of it. Liver was not palpable. Blood pressure was 150/90 although she had lower readings in the past. She never was hypertensive. Urine contained albumen in traces. No pus, no dextrose, no bilirubin were found and the centrifuged sediment failed to reveal any pathology.

April 2. Patient had severe attack last night which lasted

over 4 hrs. First those examinations were undertaken, which had been omitted during her previous x-ray work-up. On examination of the cardiac region a *hiatus hernia*, with about one fourth of the stomach being thoracic, was found, together with a marked, though not excessive *cardiospasm*. There was no food residue in the lower esophagus. Considering all facts, the present suffering seemed not to be caused by or correlated to the presence of the hiatus hernia or of the cardiospasm.

April 3. Last night she had agonizing pain. Morphine-atropine, demerol, parenterally, gave only slight relief.

Patient was given barium enema. The colon, from the splenic flexure aborally revealed an *unhastrated, sausage shape* with fairly wide and uniform lumen. At later observations (4 days later) this aboral segment was found to be spastically contracted to thread-like appearance (*colospasm*), an indication of good functional and of normal structural condition. The transverse colon was normal, well haustrated. The cecum and ascendens were wide and large, with normal haustration and mucosal foldings. The vermiform appendix looked widened, clubbed, with a pear shape and took up barium readily, show-

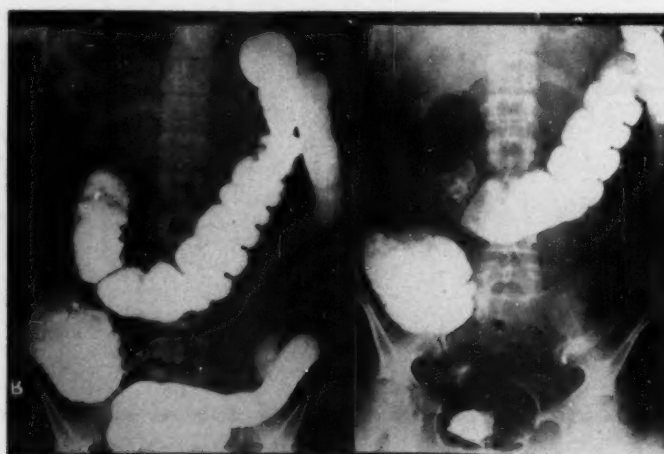


Fig. 3: Two films taken of the colon. The aboral half of the colon is unhastrated, sausage shaped, although the ulcerative colitis was cured, in clinical sense, for over ten years.

The appendix is club-shaped, with wide lumen and free movability.





Fig. 4: Film taken during the painful period of a choledochus stone impaction, 3 hrs. after barium intake. The 1st, 2nd and part of the 3rd portion of the duodenum is distended, greatly widened. Obstruction pattern in the 3rd portion of the duodenum. Passage through the stenosis is greatly slowed down.

Cecum contains some residual barium, after its intake 4 days ago.

ing free movability. The cystic widening or degeneration represented possibly a *mucocoele*, as its x-ray appearance.

*April 4.* Patient failed to come on account of agonizing epigastric pain, more severe than ever.

*April 5.* At this time Levine tube was inserted on fasting stomach. Patient vomited a large mass of thick gastric content. It was found that nearly 24 hours ago patient had eaten some mashed carrots and crackers, which was the only food she had ingested during a full day. The vomited mass, about four ounces, represented nearly quantitatively the food taken the day before. The inspissated mass did not yield even a few cc. fluid, on filtering. Congo reaction was slightly positive. The microscopic specimen failed to show any pathological elements, such as RBC, WBC, sarcinas, Boas-Oppler bacilli, or smaller motile bacteria, saccharomyces, etc. There was no abnormal smell, color or odor noted. About 75 minutes after Ewald's test breakfast practically the total amount ingested was recovered; this content was thick, poorly digested as that in achylia gastrica. There was no free HCl. The microscopic specimen was negative, again.

*April 6.* For the last two days pain was continuous. Patient noted on the previous day that her urine turned dark and it gradually grew darker. On examination it contained bilirubin in tremendous amount. The albumen was more than heretofore. Temperature was 100 F. (orally).

At this time we made an x-ray examination of the G. I. T. The barium, to our great surprise, freely entering the duodenum stopped at its third portion. The duodenal cap and the descending and part of the third or transverse segment showed maximal dilatation, with a width, reaching that of a colon. The outline of the duodenum remained throughout smooth and rounded; on the ring-like, concentric narrowing no indentations, irregular outline or worm-eaten appearance were noted. X-rays were taken at frequent intervals, during the 3½ hours observation. The obstruction pattern remained practically identical. When compression was applied to the abdomen the intestinal coils were pushed aside and the obstruction pattern was more clearly visible. The barium trickled through the stenotic ring at a greatly diminished rate, so that even after three and a half hours only moderate amount of barium entered the jejunum. (From the previous barium fillings, 3 and 4 days ago, some residual barium was still noticeable in the cecum, and the descending colon appeared maximally contracted, at this time (colospasm).

*April 7.* Last night pain subsided. Temperature was 99.8 F. (orally). The urine contained less albumen and the bilirubin content was greatly diminished. The dextrose reaction appeared now, after KH intake, as strongly positive.

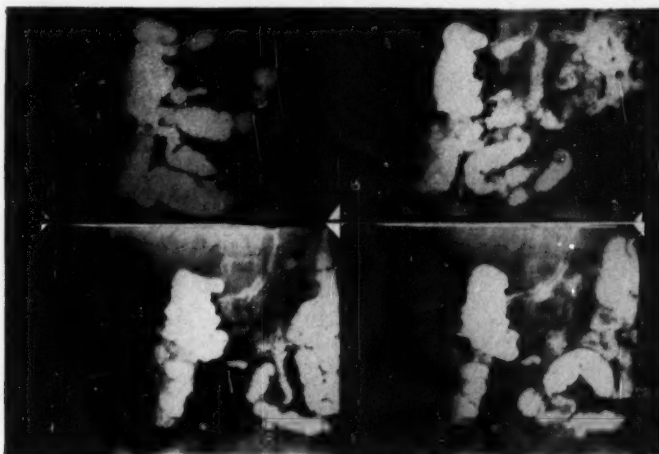


Fig. 5: 4 films taken, 2 to 3½ hrs. after barium intake, during the painful seizure, due to impaction of a choledochus stone.

They all show, nearly alike, obstruction in the transverse segment of the duodenum. Orally, the duodenum is maximally dilated, aborally, from the site of obstruction, the barium passes through only in narrow stream. Cecum contains some residual barium, after its intake 4 days ago.

At this stage the assumption of impaction of the common duct by stone seemed to be well justified. The recurring, severe painful attacks, culminating in continuous pain of several days' duration, the slight temperature, the appearance of bilirubinuria with glycosuria were all signs of this condition, even though backpressure through the obstructed duodenum might have affected both the common duct and the ductus Wirsungianus to a certain extent, even in the absence of a stone in the choledochus. This mechanism was less probable.

At this time the presence of two surgical conditions was established. Both the duodenal obstruction and the stone impaction in the choledochus required immediate surgical consideration. Patient was presented to an experienced abdominal surgeon, associated with one of the finest hospitals of this city.

April 8. Patient was to be admitted to the hospital, today. However, we arranged for her to stop at my office before entering the hospital. A recheck on the bilirubin and dextrose content of the urine and a recheck on the duodenal obstruction picture seemed to me mandatory, especially in view of the fact that the patient has felt well since the second day.

When patient arrived, she felt and acted perfectly normal. The urine passed proved to be free of bilirubin and glucose and the albumen reaction was less marked than heretofore.

The real surprise came with reexamination of the G. I. T. with x-ray. Now, the barium entered and passed through the duodenum in a perfectly normal way and appearance, without evidence of any delay. The flaky jejunal coils were visualized within very few minutes. Stomach, duodenum and small intestines all proved perfectly normal. Within 30 minutes the entire small intestine was visualized, while previously even after 3½ hours the barium did not pass through the jejunal coils.

This unusual change in the G. I. T. x-ray showed unquestionably that the previous obstruction picture must have been a functional, reflex manifestation during the stone impaction of the choledochus, the diagnosis of which seemed to be definite, now. The obstruction pattern promptly disappeared as soon as the attack was over.

The surgeon has been informed about this favorable turn in the x-ray findings and about the change in the entire situation and improved outlook. Patient has been informed and advised accordingly. She was made to understand that the duodenal obstruction proved to be functional only and that the stone passed and with it the stone attack. She understood also that there was no telling whether that signified

a final riddance from stones altogether, or only a temporary relief, in which latter case stone or stones harbored in the duct, now in quiescent state, may at any later date play havoc with her again, since, she enjoyed completely free intervals many times during the past six months.

April 9. Patient called by phone from the hospital stating that she is feeling perfectly well. This was the third day in succession that she enjoyed a respite from pain. She was told that if she is ready to risk a possible new attack in the future she could leave the hospital without undergoing the operation. She understood that in view of the fact that the stone gave no x-ray shadow, it would be speculative whether she still had or did not have any stone left in the duct. If not, the surgeon would find the common duct empty.

The decision was left to her, as to whether she still wished to undergo surgery, or would prefer to avoid it. First, she decided to go home and she so notified the house physician and also the attending surgeon. But at the last moment she changed her mind upon learning that admission to the hospital may in these days take as long as six weeks and having hospital accommodations available, she decided to stay and go through with the operation, now, rather than to take a chance of a recurring attack.

#### OPERATION

Operation was scheduled for 2:30 p.m. Adhesions between the lower edge of the liver and the adjacent structures were freed or removed. The common duct was exposed with its thickened wall. At first it looked as if the surgeon palpated stone in the choledochus; but this proved to be a fallacy. The duct was tested for patency by probing and the duct seemed to have free passage. A tube was inserted, which later had to be abandoned. Some pancreas tissue for biopsy was secured.

There was more bleeding encountered than expected. The bleeding, first from the site of biopsy and later also from other sites of the parietal peritoneum as well, gradually got worse, until it practically got out of control. I could not help feeling very uneasy about this situation and after the operation was finished around five o'clock, kept worrying about a possible after-bleeding into the abdominal cavity.

It took less than two hours when the not unexpected emergency arose. Patient looked exsanguinated, her pulse was filiform and hardly palpable and no blood pressure could be registered. Oxygen, transfusions and infusions were supplied in abundance. On opening the abdomen it was found filled to capacity with fresh and clotted blood. In the surgeon's

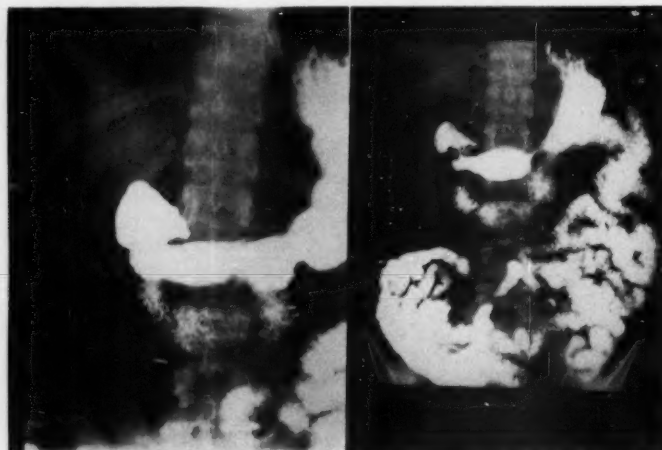


Fig. 6: The day following the attack, due to choledochus stone impaction, when patient was fully recovered, the duodenal obstruction pattern promptly gave way to a completely normal G. I. finding

A: The barium, 5 minutes after its intake freely entered the jejunum. The duodenum was found completely normal.

B: 30 minutes later nearly the entire small intestine is already filled with barium. The passage is fully restored.

opinion the source of the bleeding was mostly the site of biopsy, although numerous places of the parietal peritoneum oozed abundantly. Bleeding was profuse, with blood flowing at times and at places nearly in streams. Its control seemed to be infinitely difficult as the tissues were already friable and at places lacerated, with some parts of the mesentery and omentum showing extensive hemorrhagic areas. When the bleeding seemed to be controlled, as best as it could be, the abdomen was to be closed. I openly expressed my fear that the hemostasis might again not prove quite satisfactory. But the suturing of the abdominal wall proceeded in the belief that everything possible had been done. The closing of the peritoneum was still in progress, when the entire field was again flooded with fresh blood and reoperation had to start anew. The abdominal cavity was once more the scene of profuse continuous bleeding. Masses of fresh and clotted blood had to be removed again. Transfusions and infusions were continually administered through the veins of an arm and leg simultaneously. Patient looked extremely pale, exsanguinated without any registration of any blood pressure and pulse, now, for hours. When oxygen was suspended for a few seconds, breathing became shallow and at times it looked as if it had stopped altogether. The technical difficulties in controlling bleeding and clamping vessels increased, as the tissues became more friable, imbibed with blood or suggillated, probably partly due to lessened blood supply as a result of multiple ligations. More tissue laceration developed, especially in the mesentery. In this ominous situation the abdomen was closed again, now the third time, amid despair, slight hope and great anxiety, because the tissues could not be completely dried and some slight oozing was still noticeable.

Patient was kept on the table and everything was held in readiness in the event a new reoperation would be required. Pulse and blood pressure did not return and the bloody drain from the abdomen soon signified that the time was ripe for the fourth laparotomy.

At that time, at the request of the family, a consulting surgeon was called in, the head of a parallel service. Now, the two master surgeons went in again, only to find a repetition of the previous situation. Tremendous amount of blood was again evacuated, and still more syphoned off in order to expose, see and control the bleeding at its source. Packing under considerable pressure was applied, and this seemed to stem the bleeding, here and there, but new bleeding sources constantly aggravated the situation. It would hardly be believable that the control of bleeding, of some barely discernible and understandable origin, by two expert surgeons with all their staff, in one of the finest hospitals of this great metropolis and with all the facilities of modern surgical and medical skill and technique should encounter such nearly insurmountable difficulties.

After 2½ hours of heroic effort, when nearly all hope that the situation could be mastered, was gone, the bleeding at last seemed to have gotten under gross control. It seemed hardly believable, at this stage. The pulse returned and the blood pressure registered a reading around 115/80. The abdomen was closed anew, for the fourth time. It was now after one o'clock a.m., more than 10 hours after the start of the first operation.

During this time there were at least twenty-two pints of blood transfused and the amount of the intravenous infusions (saline, dextrose, aqua), might have run into another similar figure. All in all the blood loss might have been estimated at the fantastic figure of about 40 or 45 pints (blood, as diluted with infusion fluids).

Postoperatively patient received at least four more pints of blood, with possibly a corresponding amount of intravenous fluids.

April 11. The day following the operation patient looked unusually well. There was no fever, the pulse was good, 72 per minute, and the blood pressure was around 140/80. She was able to take and retain some fluids. The choledochus drained freely. The abdominal drains delivered blood in small quantities only (several ounces). Her exsanguinated appearance gave way to full colored countenance and the hemoglobin was in fact above normal (15 gms.).

April 12. Patient was in great distress. Respiratory dif-

ficulty of inspiratory type, cyanosis, full flushed face and anxiety were in evidence. It looked as if the system was overloaded with excess blood. The lungs were filled with moist rales. The pulse was 120, full and pounding, the blood pressure rose and the temperature registered 103 F., which rose the same evening to 105.6 F. The hemoglobin surpassed 16 gms.

It was apparent patient had developed a left ventricular failure, due to increased blood volume, as a result of the system being overloaded with blood and other fluids. Intravenous medication had to be stopped, venesection ordered and mercurhydrin and digitoxin were administered.

It seemed as if the assigned medical consultant and attending physician did not exercise vigilance and good judgment in full measure and did not take the necessary steps vigorously and commensurately in consideration of the extreme emergency which existed. The intravenous administration was not fully stopped, the venesection proved to be less, much less than half measure and the too cautious use of mercurhydrin, the miracle drug in these conditions, deprived the patient on account of some unwarranted fear of its potential toxicity from the benefit of its maximal therapeutic value. In desperate conditions desperate measures may be indicated, and they were not fully utilized here, outside of the fact that the proper execution of the proper measures required in this case could by no means be classified as desperate.

April 13. There was definite improvement following measures of combatting left ventricular failure. However, and in spite of that, the hemoglobin was still rising until it reached the figure of 18.1 gms., and the blood pressure rose continually until it reached 175/130 and the respiration was, though improved, still far from satisfactory. Temperature hovered between 103 and 104 F.

April 14. General condition deteriorated in great measure and amid signs of increasing dyspnea, plethora, polyglobulia, hypertension the patient passed away.

## COMMENTS. DISCUSSION

### 1. *Pancreas biopsy.*

Although no clear indication existed for diagnosing or even suspecting pancreas carcinoma, a pathohistological examination for the proof or disproof of its existence can be considered a routine procedure.

Result of this biopsy for carcinoma was negative.

### 2. *The biliary system.*

The biliary problem here related to the common duct and its transient impaction by stone. This problem is bound up with the postcholecystectomy syndrome-complex. This is a complex of heterogeneous morbid conditions. It develops especially after an injudicious removal of a good-functioning gall bladder, whereby the system is subjected to a sudden change caused by the loss of function of this active organ. Symptoms usually develop soon after surgery. Anything developing as late as 7 or 8 years after this operation could hardly be considered as a postcholecystectomy syndrome. Whatever the case, one has to search for the underlying cause and pathology in the specific instance, anyway.

Among these causes Upham puts the erroneous preoperative diagnosis responsible as the No. 1 cause for the postcholecystectomy syndrome. In a series of 1000 cases in Vichy, France an inconceivably high figure of 66% was found to belong to this group. (G. F. Bonnet, Upham).

The choledochus stone ranks second in sequence. Presence of the choledochus stone is, par excellence, prone to produce the postcholecystectomy syndrome



complex. Whether it was left in during the operation, or developed thereafter often remains a question of academic interest only, as in this case. During operation once in about every four cases a choledochus stone is found, often undiagnosed, and in about 80% of such cases without direct x-ray evidence. Cholangiography performed at the operation would be diagnostic in most cases, when routine x-ray examination fails.

The biliary attack, at first intermittent, finally culminated in a sharp painful siege of a week's duration. The sudden appearance of the bilirubinuria with icterus and glycosuria without diabetes, their transient character followed by their prompt and sudden disappearance makes the diagnosis of a stone impaction of the common duct as good as assured. The intermittency and severity of the painful attacks speak also for a common duct impaction by stone, and against any other causative agent. This course of events, like an experiment in vivo can be considered characteristic of a transient stone impaction which practically rules out the probability of other etiology.

In the presence of other etiological factors, such as tumor, cyst, glandular pressure, adhesion and ligament, etc., a persistent and gradually increasing jaundice and glycosuria is to be expected in line with the progressive tendency of the underlying pathology.

The same holds true for an organic non-calculous stricture of the common duct, which may develop in a traumatized choledochus either postoperatively or as a result of adhesion, between the inflamed gallbladder and the common duct (Behrend, Poppel-Jacobson-Smith). Upham quotes Bryant to the effect that all cases who had cholecystectomy, possessed adhesions (perivisceritis) in the subhepatic area.

In the case of stone impaction the stone is either large enough to obturate the lumen, or if it is small, it may effect occlusion by its added reflex spastic action upon the enclosing mucous membrane. The presence of the impacting stone in this case was assumed to be in the intraduodenal portion of the common duct, a 15 mm. segment, because stone impaction only at this site would produce pressure simultaneously on both the common duct and the ductus Wirsungianus.

The diagnosis of the choledochus stone is by no means always an easy one. Not only can its clinical appearance be doubtful or elusive, but according to Bockus "a definite diagnosis can not be achieved in the majority of cases with residual common duct stone by x-ray and diagnostic biliary drainage; and the surgical evidence of choledochus stone by probing, suction, intubation are very unsatisfactory." If all these manipulations fail, there are other special technical considerations to assure oneself that the common duct has been freed of stones (Wangensteen).

Bockus quotes Mirizzi of Argentina, who found choledochus stone in 26.6% during cholecystectomy, proven by cholangiography. Crump in Austria found this incidence in 24%, in the U. S. A. Lahey in 25%, Behrend in 20%, etc. Mallet-Guy of France found in 100 consecutive cases of cholecystectomy that 38 had diseased ducts.

All that related to our case would suggest that even after the probing of the duct some reasonable doubt still may exist, as to the possibility of a residual stone being left in the common duct.

3. *Duodenal Obstruction.* a)—*Nomenclature: obstruction vs. stasis.* Certain authors use the term duodenal stasis as synonymous with duodenal obstruction and occlusion. That may give rise to confusion. Obstruction as a rule develops with a structural narrowing of the lumen, while stasis means only delayed emptying, from whatever cause. Obstruction always involves stasis, but stasis is not necessarily caused by obstruction. Obstruction is practically always structural. Stasis may or may not have any organic basis. The two expressions should not be used as synonyms. Feldman applies the term of duodenal stasis to all forms of obstructions or occlusions of the duodenum, as detailed in his book. Again, in his paper on the chronic intermittent duodenal stasis (Friedenwald and Feldman) he uses the term of stasis for the slight transient motor disturbance in some duodenal segment, for slight delays, bordering on normal. Bockus uses the term stasis only for slight delay in emptying, delineating it from obstruction. He emphasizes that stasis is not a clinical entity and should not be handled as such. Walter L. Palmer applies the term also only to mild cases, considering it to be a normal variant in lanky, lean persons, who exhibit certain characteristics, noted by fluoroscopy (churning, puddling, reverse peristalsis). He groups obstruction and occlusion apart from stasis. Markovics uses stasis in restricted form, when the bulb fills normally, only its emptying is delayed. Portis does not use the term of stasis at all in his book on Diseases of the Digestive System, nor do Shank and Kerley in their excellent new monographs.

b)—*Frequency.* According to Feldman duodenal stasis is very rare. He quotes to this effect Jewett who found it only 15 times among 30,000 general hospital admissions; nearly the same ratio is quoted by Ratkoczy in an obduction material, i.e.: 0.06%. I should like to correct this statement to the effect that stasis, in the sense of obstruction, is by no means so rare.

c)—*Classification.* Obstruction may be persistent or intermittent (Feldman). In persistent obstruction the damage is permanently present, it is structural and often progressive. In the intermittent type the stenotic symptoms may come and go and return again automatically or on positional changes, etc., according to the causative agent. The chronic intermittent stasis of Friedenwald and Feldman occurs usually during the bilious migraine attacks of the neurotic type of middle aged women. They concede that the duodenal x-ray changes are slight, delay of the barium is so moderate as to vary little from normal.

d)—*Functional elements. Associated conditions.* According to Feldman duodenal stasis also may develop on functional or reflex basis. This would occur in conditions which he defines as the associated conditions to duodenal stasis. Feldman states that "the associated conditions found in duodenal stasis are peptic ulcer, gastric dilatation, cholecystitis, pancreatitis and mucous colitis." He found, as did other authors, quoted by him (Codman, Sloan, Wilkie, Friedenwald-Feldman, etc.), frequent association of these conditions with duodenal stasis.

As against this I quote Bockus who in his critical analysis on this subject, states: "which is the cart and which the horse in the combination of peptic ulcer and



duodenal stasis has not been established," and again: "there may be no cause-effect relationship, certainly none has been proved to exist." The same way he separately analyzes the case with duodenitis, cholecystitis, pancreatitis, mucous colitis, etc., and comes to the conclusion that there is no convincing evidence of relationship of cause and effect between the duodenal stasis and any of these diseases. That would put a quietus to this problem because no evidence for such association has been established.

This is in reply to the question whether duodenal stasis can or can not develop on functional or reflex basis. I quoted Bockus because he, with his clear and frank elucidation on this important question, masterfully analyzes the issues involved and his comments happen to be in full conformity with and also express my personal views on this subject.

e)—*The spastic and paralytic obstruction and occlusion.* Here there is some functional involvement, especially in the spastic type. However, this is not an associated condition, it is not a functional or reflex phenomenon, but the functional disturbance is the morbus ipsa.

The *paralytic or adynamic ileus* is the more important of the two. Its occurrence postoperatively, in peritonitis, in severe infections in the abdomen, occasionally even in pneumonia, or in severe painful stone attacks, in spinal injury, in mesenteric thrombosis and embolism are long known. The term "functional obstruction" as occasionally used (Bockus, Portis) seems to me not a fitting designation, as there is no obstruction of the lumen, latter is open and wide, but there is a loss of power of motility, which serves as a cause for the paralysis; nor is the paralysis functional, inasmuch as it is brought on not by any specific function, but rather by the lack of it. The paralytic theory has been also challenged by recent observations, on ground of which this condition may be considered due to hyperactive sympathetic influences, and is called therefore also as "reflex inhibitory ileus" (Ochsner-DeBaakey).

The *spastic type* of the functional obstruction, called also spastic ileus (Murphy, Zimmerman, Bockus) is not a clear cut clinical entity (Bockus). The extensive threadlike contraction of the colon, occurring often with neurotic individuals, its sudden demarcation from the normal segment, is a very characteristic feature. This "colospasm" has been frequently observed by author, likewise, either with neurotic individuals, or as an accompanying reflex spasm in the presence of various morbid conditions, among them a cancer of the G. I. T., at any segment, a peptic ulcer, pathological gallbladder or appendix may be mentioned. Colospasm in the author's observation has always been found as an innocent transient spastic phenomenon. If there ever was any doubt as to its significance, in any questionable case, a barium enema instantly answered the question by promptly returning the colon to a normal size, shape and function. Colospasm never caused stenosis or motor disturbance in the author's cases. How such cases were subjected to operation, with a mortality of 31% is beyond comprehension. In the case presented here the aboral colon also showed typical reflex colospasm without any significance on the films taken 3 or 4 days after the ingestion of

barium. It is still less conceivable how these spastic contractions, or for that matter any spastic contraction, would persist also during and after operation, anesthesia, and be demonstrable even on the post mortem table (Körte).

The term of spastic ileus for colospasm is not fitting. Colospasm is not an ileus, it is merely spasm, such as frequently observed over other segments of the irritable G. I. T., or in any other hollow, muscular organ, without ileus symptoms. If one speaks of spastic ileus, volvulus and intussusception are the ones to be rightfully grouped with it. The case presented here might be classed as a spastic obstruction of reflex origin.

f)—*Localization.* The most common site of duodenal obstruction seems to be the duodeno-jejunal junction where congenital as well as acquired morbid conditions may cause persistent or transient obstruction, due as a rule to kink or angulation. Among the causes of occlusion or obstruction at this juncture besides congenital anomalies, Treitz's hernias, intrinsic benign and malignant tumors, intussusception, extrinsic factors, such as cancerous or tuberculous glandular masses, pressure from diseased or enlarged pancreas or kidney, adhesions, bands and ligaments, etc., play the etiologic role. The resulting obstruction in these cases is usually persistent and of progressive nature (Carman, Assmann, Schlesinger, Meyer, Stierlin-Chaoul, Feldman, etc.).

Bockus considers the third or transverse portion of the duodenum as the most frequent site of obstruction. This location is identified with the course of the arteria mesenterica superior, as it emerges from the aorta, behind the body of the pancreas and rides in front of the third portion of the duodenum, thereby this transverse segment of the duodenum becomes enclosed between the aorta from the back and its branch, the mesenteric sup. artery, in front.

Bockus giving a historical review of the role of the mesentery in the precipitation of this ileus since Rokitsky first suggested in 1849 that the mesentery might be responsible for certain cases of duodenal stasis and dilatation, comes to his own conclusion, whereby this arteriomesenteric ileus is, in his extensive experience the etiologic factor in approximately 75% of all the cases of duodenal obstruction. He considers all other types rare and difficult to diagnose.

Through similar mechanism the vena mesenterica superior may become engorged postoperatively and this may exert pressure on this very same duodenal segment, causing constriction of the lumen. This has been considered as the cause of postoperative acute gastric dilatation (S. A. Portis).

According to Albrecht (Bockus, Feldman) the circumference of the transverse portion of the duodenum at this site is normally flattened and thereby predestined to become completely compressed in the presence of aggravating factors. Among these factors lordosis of the spine, narrow angulation of the superior mesenteric artery, rigidity and sclerosis of the vessels, especially in association with splanchnoptosis, enteroptosis, low mobile cecum, redundancy or atony of the duodenum may be mentioned. The traction produced will drag down the mesentery with their vessels therein, resulting in compression of this duodenal

segment. All that is of course more manifest in the erect position. In fact, the change into a recumbent or especially a knee-elbow position may abruptly act as a decompression (Hans Helmer, Feldman, Ratkoczi).

Obstruction may develop at any other segment. Supra- and infrapapillary tumors—cancer and lymphoblastoma—obstructive large gallstone lodged in the duodenum after perforation of an adherent gallbladder, are among the causes of obstruction in the descending portion of the duodenum. Rarely a post-bulbar duodenal ulcer in its late stage may lead to obstruction at this particular segment, although the obstructive tendency at this location is not great (Arthur Finkelstein).

Obstruction at the duodenal bulb or at the site of its transition to the second portion is a late development in ulcers of this region, not unlike the pyloric stenosis which develops from peptic ulcer of the pyloric region. Fibrosis, scar, retraction, sclerosis and shrinkage superimposed by accompanying spastic components add up to the development of the characteristic picture of duodenal deformity. In the early stage the spastic elements, later the structural changes, are in the foreground and finally partial or complete obstruction may be the feature.

In all these cases the segment proximally to the obstruction is greatly dilated and is densely filled with the opaque material. No mucous folds are visible unless the intraluminal pressure is relaxed. Then the valvulae conniventes of Kerkring unfold. This is not present in the first portion, but always demonstrable in the third segment, while the second may be the seat of some transitional picture more resembling that of the third segment's structural pattern. Carman thought that these plicae circulares do not change their basic pattern unlike the gastric mucosa. Farsell however was able to demonstrate changes in the mucosal folding attributed to the function of the muscularis mucosa whereby the transverse folding may transform into oblique or even longitudinal patterns.

All these descriptions refer to radiological demonstrations of changes of purely structural character.

g)—*The role of the functional elements.* There are also functional changes which are amenable to roentgen visualization. It has been noted and known since the early roentgen era that certain pathological conditions, esp. in the gallbladder or appendix, may reflexly produce functional changes in some distant organ. Among them, par excellence, the roentgenologically demonstrated spasms in the stomach, colon and rarely in the duodenal bulb attained some prominence. Furthermore other types of functional changes were observed, like a deep spastic incisura of the greater curvature of the stomach pointing like a finger to the site of an ulcer of the curvatura minor, on the same level of the opposite side. In other cases the role of the spastic elements in the bulbar deformities was described. Assmann, Carman and others noted some reflex spasm in the first or second portion of the duodenum in diseases of the gallbladder or the pancreas. While Cole, Carman, George and Gerber, among others, observed functional changes over the bulbus duodeni without signs of simultaneously demonstrated ulcer, Akerlund denied the existence of these functional elements unless there was some organic basis, such as

ulcer, present. Holmes and Ruggles considered the reflex changes on these hollow organs so important and characteristic that they went so far as to suggest that when gallbladder disease is suspected a routine G. I. T. examination should be undertaken, in order to determine the presence or absence of reflex gastric disturbances, such as spasm or stasis, a suggestion which would hardly find followers today.

h)—*Own observations on the role of functional elements.* In the author's own observation a reflex hour-glass incisura of the duodenal bulb was described as a product of a double cancer of stomach, corroborated by operation. In other cases of his series extensive spastic contractions were noted along the transverse and descending colon, on reflex basis, the lumen of the colon appearing in filiform, stringlike line. On barium enema a sudden reappearance of a normal colon was in evidence, proving the spastic nature of this filiform appearance, and ruling out an organic stenosis. Such colospasm never interfered with the propulsion of the content, or the motor power of the organ. In the same publication the author referred to cases where the terminal ileum showed reflex spasm, without any local pathology, in differentiation of the stringsign of Kantor, in terminal ileitis. Also reflex spasm of the second portion of the duodenum was observed, either in a straight thin line, or appearing more in the shape of a corkscrew. Still in another publication the author described spastic changes in the vermiform appendix together with diverticulum-like widening of the remaining segments of the appendix, with varying shapes. While this was the observation during an emotionally disturbed state in a neurotic young girl, later during an adjusted period the appendix resumed a perfectly normal appearance, with uniformly wide lumen.

i)—*Structural vs. functional elements in the present case.* Present observation was of entirely different significance. Here the functional disturbance produced changes interfering with normal motility. The changes were identical with those of any organic obstruction. The barium could only trickle through the stenotic ring, so that even after three and one-half hours' time only the jejunum was visible and not the ileum. Proximally to the obstruction a maximal dilatation with considerable motor disturbance completed the picture. The width of the bulbus and descending duodenum reached that of an average colon. During the three and a half hours' observation time films were taken in frequent intervals, first on standing, later in prone position. The type and degree of the obstruction remained throughout unchanged. How much longer this obstruction pattern lasted could not be stated with any accuracy.

During the time of x-ray examination the stomach emptied normally. The distention started at the pyloric ring. The previous day, however, when a 24 hour gastric retention was noted by gastric tube, after a very little food intake, the x-ray demonstration at that time undoubtedly would have revealed this motor insufficiency of the stomach proper. Both the clinical as well as the radiological evidences of the gastric and duodenal obstruction proved to be transient, demonstrable only during the period of acute stress, when the common duct was impacted by stone. When

this state was over the G. I. T. and its motor power promptly returned to normal without any indication of the previously demonstrated serious motor disturbance.

## SUMMARY

The case presented has been that of a 49 year old female who eight years after cholecystectomy developed a clinical picture considered typical of a choledochus stone impaction. Patient had no symptoms during the intervening eight years suggestive of any biliary disease. During the time of stone impaction the patient developed the clinical picture with its roentgenological manifestations of an obstruction of the third portion of the duodenum with subsequent gastric and duodenal retention. After the biliary attack passed, the obstruction disappeared, and the gastrointestinal function promptly returned to normal. The obstruction of the duodenum, at its third portion proved to be a reflex manifestation due to the impaction by stone, and not a structural development.

During a relatively small operation, namely the search for or removal of a choledochus stone, the most unusual and uncontrolled bleeding developed at the hand of a master surgeon, in one of the very best known and equipped hospitals of this great metropolis. The abdomen had to be opened four times in eleven hours, the time required for these four operations. The blood loss amounted to an estimated 40 or 45 pints.

Four days after the operation the patient passed away with symptoms of a left ventricular failure, due to increased blood volume, as a result of the system being overloaded with blood and other fluids, causing respiratory difficulties, high blood pressure, polyglobulia with a patient who during the operation for about eight hours had no pulse, no measurable blood pressure and throughout this time looked like one completely exsanguinated.

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## ABSTRACTS ON NUTRITION

MOLLIN, D. L. AND ROSS, G. I. M.: *Serum vitamin B<sub>12</sub> concentrations of patients with megaloblastic anemia after treatment with vitamin B<sub>12</sub>, folic acid or folinic acid.* Brit. Med. J., Sept. 19, 1953, 640-645.

The serum vitamin B<sub>12</sub> concentrations of patients with pernicious anemia in relapse rose from low pre-treatment levels to within the normal range after single intramuscular injections of 20 to 1,000 micrograms of vitamin B<sub>12</sub>. Concentrations were within normal range for from 6 to more than 18 days after injections of 20 micrograms; from 2 to 22 days after 40 micrograms; from 11 to at least 35 days after 80 micrograms; from 11 to at least 48 days after 160 micrograms; from 39 to 98 days after 320 micrograms, and from 34 to at least 58 days after 1,000 micrograms. Megaloblasts reappeared in the marrow when the vitamin B<sub>12</sub> serum concentration fell below the normal range.

The authors, however, suggest that, in treating a case of relapse, as much as 5,000 micrograms be given in the first two weeks, not only to supply enough of the vitamin for blood formation but also to replenish the greatly depleted tissue reserves.

It is estimated that a normal person's body as a whole contains from 1,000 to 2,000 micrograms of vitamin B<sub>12</sub>.

The serum vitamin B<sub>12</sub> concentrations of patients with various megaloblastic anemias were not altered by treatment with folic acid or folinic acid.

NAKKASH, B.: *Biochemical changes in the blood in diabetes mellitus.* Jour. Med. Professions Assn., Baghdad, 1, 1, March and June 1953, 27-30.

The chief alterations in the blood in diabetes are listed with brief commentaries. These include decreased respiratory quotient, hyperglycemia, decreased carbohydrate tolerance, lipemia, ketosis, acidosis, hypochloremia, hemoconcentration, reduction of fixed base, decrease in serum potassium and hypoproteinemia.

GUPTA, C. P. D., CHATTERJEA, J. B. AND BASU, P.: *Vitamin B<sub>12</sub> in nutritional macrocytic anemia.* Brit. Med. J., Sept. 19, 1953, 645-649.

Twenty-one cases of nutritional macrocytic anemia were treated with vitamin B<sub>12</sub> given intramuscularly and seven cases received the vitamin by mouth. Initial improvement in 64 percent of cases was good but sustained remission was obtained in only 23 percent. Even in the latter cases macrocytosis tended to persist. Folic acid and crude liver extract evoked adequate or better response in most cases not showing sustained remission with vitamin B<sub>12</sub>. The authors feel that their studies indicate that nutritional macrocytic anemia represents deficiency of both folic acid and vitamin B<sub>12</sub>, deficiency of folic acid being the major and primary factor. Lack of vitamin B<sub>12</sub> is the minor or secondary factor in most cases.

HARRISON, M. T. AND MERCER, R. D.: *Vitamin A intoxication.* Cleveland Clin. Quart., 20, 4, Oct. 1953, 424-429.

A case of vitamin A intoxication in a 28 month old boy is reported. The chief clinical manifestations were hyperirritability, cheilosis, pruritus and swelling along the ulnas and along the fifth metatarsals. X-ray showed subperiosteal new bone formation. High blood levels of vitamin A helped to confirm the diagnosis. Prompt relief of symptoms followed the withdrawal of vitamin A. Almost since birth this child had been given daily as much as 1 to 2 teaspoonfuls of Oleum Percomorph (Mead-Johnson). One teaspoonful of this concentrate provides 200,000 units of vitamin A and 30,000 units of vitamin D.

INGLE, D. J., MEEKS, R. C. AND HUMPHREY, L. M.: *Effects of environment on diabetes.* Diabetes, 2, 2, March-April 1953, 122-124.

It would have been expected that stress (such as that produced by marked lowering of the temperature of the atmosphere) would have worsened the condition of diabetic, depancreatized male rats, because one would expect stimulation of the adrenal cortex. However, the level of glycosuria decreased during exposure to cold, although there was weight loss and increased excretion of non-protein nitrogen. It is possible that emaciation itself may have caused a lowering of the blood sugar. Furthermore, gluconeogenesis may have been accelerated in these animals so that the extent of utilization of sugar cannot be determined by measuring changes in the level of urinary glucose alone. The problem deserves further study.

ROHN, R. J. AND BOND, W. H.: *Observations on some hematological effects of Cobalt-iron mixtures.* Journal-Lancet, Aug. 1953, 317-324.

A cobalt-iron preparation containing 70 mg. of ferrous sulfate and 40 mg. of cobalt chloride for each 0.6 c.c. of aqueous solution was used in the treatment of 23 infants with uncomplicated nutritional iron deficiency anemias. In 2 adults and one infant with moderately severe to severe panmarrow hypoplasia, cobalt chloride alone was given in 120 to 200 mg. dosage per day. No toxic reactions were noted. Cobalt caused markedly increased levels of circulating red cells, white cells and thrombocytes in the majority of patients, and in some there was a significant elevation of circulating eosinophilic and basophilic leukocytes. Two of the patients who responded appeared to be instances of aplastic anemia.

PENNINGTON, A. W.: *Treatment of obesity with calorically unrestricted diets.* J. Clin. Nutrition, 1, 5, July-Aug. 1953.

Pennington summarizes his scheme of reducing fat persons by permitting them to eat the meat they wish (not less than 8 ounces per meal) plus one-quarter of

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this weight of fat meat. Carbohydrates are restricted to 60 grams or less per day. Vigorous exercise *before* breakfast is part of the plan. The ketogenesis which results seems to be the key to using up the patients' excess fat. Pyruvic acid, largely derived from carbohydrate, appears to block the metabolism of fat. No case reports are included in this article.

BARWIN, H.: *Infant feeding*. J. Clin. Nutrition, 1953, July-Aug., 1, 5, 349-354.

There is no sense in the daily, precise calculation of the caloric needs and of the percentage of the various dietary constituents in an infant's diet. Psychological evaluation of the mother and child is fundamental to the frequency of feeding. Pediatricians are agreed, in the main, that breast milk is the preferred food for infants, but a mother who does not wish to nurse her babe should not be requested to do so. In using cow's milk, simpler formulae now are used. A four-hour

schedule is good but may be altered to suit the infant, but the infant should be permitted to take as little or as much as it wishes at any one feeding. Solid foods are best begun about the third or fourth month.

BOINES, G. J.: *Nutrition in poliomyelitis*. J. Clin. Nutrition, 1953, July-Aug., 1, 5, 355-361.

In addition to early ambulation and muscle relaxation through the use of curare, Boines emphasizes the importance of a special nutritional program in poliomyelitis. The crux of this program is a high protein intake, from the very moment the patient becomes affected by the disease. By such a method the usual weight loss following the attack is prevented. Protein supplementation both by mouth and parenterally is used and calories are augmented with Lipomul® which has been found acceptable by the patients. Optimal muscle metabolism is, of course, the object in view.

## EDITORIALS

### DUODENAL ULCER AS A FIXED EXPRESSION OF PERSONALITY

If you "cure" a patient of duodenal ulcer by the usual medical methods, or by gastrectomy, you have failed to cure that intangible quality of the patient's personality which was responsible for the original development of the ulcer. Much argument continues with respect to what features of the mind or brain operate to form a duodenal ulcer. Generally speaking, most physicians regard the cause as anxiety, or else non-specific stress. Alexander persists in his view that the ulcer develops because of the suppression of the oral-dependency emotion. Whatever the actual cause, Browning and Houseworth (1) recently have made what appears to be a really valuable contribution to duodenal ulcer by showing that, following gastrectomy, there is an unexpectedly high incidence of psychoneurotic manifestations in the months following operation.

Such symptoms include hypertension, muscle stiffness, migraine, asthma, neurodermatitis, and anxiety states. Patients under medical treatment, but still with mild ulcer symptoms, did not develop further symptoms.

These facts constitute a good "plug" for the services of the psychotherapist. Such services may at times be required, because it appears that as long as the ulcer is present and causing symptoms, something deep in the soul of the patient is strangely satisfied. Nevertheless, in actual practice, many patients, following gastrectomy, do not seem to develop any other symptoms. Certainly, the operation itself frequently is life-saving.

1. Browning, J. S. and Houseworth, J. H.: Development of new symptoms following medical and surgical treatment of duodenal ulcer. *Psychosomatic Medicine*, XV, 4, July-Aug. 1953.

### THE EFFECT OF INCREASED POSTAGE RATES

Postmaster General Summerfield is pushing a bill, H. R. 6052 which, if it became law, would increase second-class postage rates by a further 40 percent—a total increase of 67 percent in about 36 months. It is natural that the Magazine Publishers Association, Inc. should attempt to thwart this increase, since it would mean decreased profits for all publishers of magazines. While we are in sympathy with the present Administration's efforts to reach a balanced budget, and while we know that, for various reasons, the Post Office Department has never been a money-making institution, we nevertheless feel that H. R. 6052 would cause considerable difficulty for small publishers in particular. Magazines, on the whole, contribute a great deal to public education, and this is why the Government for so many years has permitted a reasonable and comparatively low rate on second-class matter.

The American Journal of Digestive Diseases, while it is not a non-profit organization, has, like the Post Office itself, never been a money-making institution. The policy of the Sandfield Publishing Company has been to maintain a practical, high-grade medical journal. Furthermore, the American Journal of Digestive Diseases is now in its 20th year of publication but the *subscription rates have never been raised*. This is something of an accomplishment, requiring rigid economies all down the line. We sincerely hope that second-class rates will not be increased because, in our case at least, this would represent a definite hardship. It is quite possible that our legislators may see fit to exempt scientific journals from any increased postage rates that may be imposed.

E. Buehler, Business Manager.

## BOOK REVIEWS

RESPIRATORY DISEASES AND ALLERGY. Josef S. Smul, M. D., Medical Library Company, New York, 1953. \$2.75.

Smul thinks that the majority of upper respiratory "infections" (as we usually regard them) are not infections primarily but rather allergic manifestations. The essence of his treatment (for all of them) is cutting out of the diet completely milk, cream, cheese and sugar. Those who do not get better by this elimination, receive injections of ragweed, dust and catarrhal combined vaccine. He includes bronchiectasis as one of the diseases to be so treated. The reviewer cannot but regard with skepticism the principles described, while admitting that he has never tried such principles of treatment. Dr. Smul may be a voice crying in the wilderness of medical unbelieveables. On the other hand, he may be mistaken in some of his assumptions. In any event, we believe that a book calculated to convince the medical reader of its truth, should provide greater scientific evidence, particularly case histories. As it stands, the book is a kind of "fiat" without any logical demonstration.

SYNOPSIS OF PEDIATRICS. John Zahorsky, M. D. The C. V. Mosby Company, St. Louis, 1953, \$6.00.

The sixth edition of this deserving member of the famous "synopsis" series, maintains its excellent reputation. It is a wonderful book for the general practitioner. Anyone who carefully studies and ponders on the condensed information in its 600 pages is capable of doing good pediatrics. An appendix dealing with the management of medical emergencies is new and very helpful.

WATER, ELECTROLYTE AND ACID-BASE BALANCE. Harry F. Weisberg, M. D. The Williams and Wilkins Co., Baltimore, 1953, \$5.00.

Weisberg uses the normal and pathologic physiology as a basis for therapy. This monograph serves as a review and source book, so that the reader may have the major subject material in one volume. The essence of the material is briefly summed up in the Tables. It is a highly practical volume and should be in every physician's library.

## GENERAL ABSTRACTS OF CURRENT LITERATURE

MONSAINTEGN, A., TANRET, P. AND BERNIER, J. J.: *Humoral effects of stenoses of the pylorus in adults*. Arch. Mal. App. Digestif, 42, No. 3, March 1953.

This report has a dual purpose: the clarification of the principal data known on this question of digestive physiopathology and the study of certain problems so far not satisfactorily solved.

Its interest exceeds that of pure stenoses since, if these have become rare, the humoral effects of gastric suction and acute dilatation of the stomach raise similar problems.

The electrolytic study made was concerned with an extreme type of experimental stenosis in which spoliation was particularly brutal and differentiated—notably histaminic hypersecretion in a completely stenosed stomach. The report does not give details of the experiments carried out, but gives the conclusions drawn. Some well-known ones are concerned with hypochloremia, alkalosis; others take into consideration more recent data, notably the changes in sodium whose plasmatic variations do not correspond to losses observed in the urine and the gastric fluid and must express changes in the distribution of the extra-cellular sector towards the intra-cellular sector. The changes in potassium are also described as are the changes in the water of the intra sector towards plasma. All these mutations of electrolytes are liable to great variations depending on the composition of the gastric juice.

The water loss may be compensated for in part by

a certain *absorption of water* by the stenosed stomach. The main consequence is that a well maintained diuresis does not allow the hypothesis of a certain degree of dehydration to be ruled out. The maintenance of diuresis is in itself the cause of the electrolytic loss and notably of a loss of K which may produce a real syndrome of hypochloremia with hypokalemia and alkalosis.

In all these facts, the problem which imposes itself is that of the origin of the water lost. Certain arguments enable one to consider the immediate importance of the participation of the intra-cellular liquids which, in the most acute forms would play a most important part.

"Renal" effects of stenoses of the pylorus raise a vast and badly elucidated problem in which occur excessive nitrogenous catabolism with probable intra-cellular dehydration, renal effects of the loss of extra-cellular liquids and of alkalosis as such.

The effects of treatment are easier to understand if one bears in mind the composition of the liquids most commonly employed. The ionogram of these liquids should be studied and compared with that of plasma. The hazards of treatment are of two varieties:

either to ensure excessive diuresis by a predominantly glucose administration and without giving any electrolytes;

or to surcharge the organism with electrolytes, notably by hypertonic solutions without the necessary supply of water.

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The addition of potassium to the substitute treatment has constituted a progress whose origin (in studies of metabolism) and whose significance (at the level of the intra-cellular liquids) it is not without interest to reveal.

DEBRAY, CH. AND HARDOUIN, J. P. *Experimental exit ulcer*. Arch. Mal. App. Digestif, 42, No. 4, April 1953, pp. 452-501. Eight figures and a bibliography.

The experimental exit ulcer is the one which forms at the point where, immediately below the stomach, the gastric secretions strike the small intestine. It results from the disequilibrium produced between the attacking hydrochloric-peptic juice and the defense set up by the duodeno-pancreatico-biliary secretions and by the resistance of the wall.

1. Certain ulcers are clearly connected with the *fragility of the wall of the intestine*, whose mucous membrane, becoming increasingly less resistant as it gets further away from the stomach, will be digested by the gastric juice. The ulcer of Meckel's diverticulum is a good example of really spontaneous formation in man. It is situated on the mucous membrane of the small intestine, just at the exit of the diverticulum whose mucous membrane has undergone gastric heterotopia. Since 1932 Matthews and Dragstedt have been able to reproduce this ulcer experimentally.

2. The suppression of the buffer value of the *pancreatico-duodeno-biliary secretions* also invites an experimental exit ulcer. The suppression of the biliary secretion, especially if there is at the same time retention, as in the simple ligation of the choledoch—arouses particular susceptibility to ulcer. The pancreatic juice plays a role, but it is a less important one.

3. In order to increase the *volume, the duration and the acidity of the secretion*, the fictitious meal method was at first tried, but results were very unequal except where the general health of the animal was impaired. On the other hand, the injection of *delayed-action histamine* regularly provoked gastro-duodenal ulcers either by gastric hypersecretion or by vascular disorders. Acute duodenal ulcers set up by instilling *hydrochloric acid* into the stomach have revealed important facts: the importance of the permanence of the attack, the role of pepsin and various general factors such as acidosis and denutrition as facilitating factors.

4. *Surgical experimental exit ulcers* (Mann and Williamson's ulcer, ulcer after gastro-enterostomy) are well known to experimenters and to surgeons: if the presence of the gastric juice is indispensable for their appearance, several factors, analyzed in this report, facilitate it.

The following are the report's main conclusions:

1. In experimental exit ulcer *the presence of active hydrochloric-peptic juice is necessary*. If this juice is deficient, the ulcer is not produced even in the combined presence of other experimental factors.

2. In most cases, *various factors favoring it should be added*. Amongst these should be noted the presence of pepsin, the absence of pancreatic and especially biliary secretions, acidosis, denutrition, the existence of slight parietal lesions.

3. Experimental exit ulcer and post-operative ulcer

in man are almost identical. On the other hand, and despite disturbing similarities, it is not possible to identify experimental exit ulcer exactly with spontaneous duodenal ulcer in man.

SUERMONDT, M. E.: *Regional enteritis*. Arch. Chirur. Neerland. 5, 2, 157. 1953.

On the basis of clinical findings and animal experiments, it is possible that allergic reactions are the basic cause of regional enteritis and the occurrence or relapse following radical resection. The constantly repeated allergen-antibody reaction gives rise to allergic reactions in a circumscribed part of the intestine. This causes circulatory disturbances in the intestinal wall and angioneurotic oedema, resulting in constriction of the intestinal lumen and stagnation of the intestinal contents. As a result of the combination of these factors, the normal intestinal flora may secondarily cause an infection of this part of the intestine, which in turn gives rise to the clinical symptoms of regional enteritis. Eighteen cases were observed. If possible, clinical and radiological diagnosis should be followed by radical resection. There is no certainty regarding radical cure, as there is no means of foreseeing new allergic reactions which may give rise to relapses. In the acute stage of the affection, and at the first stage of relapse, it is indubitably justifiable to administer antihistamines in order to prevent allergic reactions, antibiotics and sulfonamides in order to control the infection, and to adhere to an elimination regime.

Franz J. Lust.

SACHS, MAURICE D.: *Visualization of the common duct during cholecystography*. Am. J. Roentgen & Rad., Th., 69, 5, 745. May 1953.

Up to the present time, pathological changes of the transduodenal segment of the common duct (sphincter of Oddi) have been diagnosed during an exploratory laparotomy, cholangiography, or at postmortem examination. Recent experience with evacuation studies during cholecystography in some instances confirmed by operative cholangiography has permitted the diagnosis to be made preoperatively thereby enabling the physician to plan the necessary proper medical or surgical therapy. A thorough understanding of the pathological physiology of the biliary tract is essential. Cholecystography should consist of multiple films taken at approximately 8 min. intervals during the first 30 minutes following fatty meal. Additional films, at varying time intervals as determined by the roentgenologist, should be taken if there is evidence of abnormal biliary function. In conjunction with this technique, prostigmine, by its action on the sphincter of Oddi, aids in the visualization of the common duct. Only in this manner can such findings as dysfunction or fibrosis of the sphincter of Oddi or compression of the common duct by pancreatitis be diagnosed by cholecystography.

Franz J. Lust.

VAN WEEL: *The importance of pancreatoduodenectomy in the treatment of tumors in the region of the head of the pancreas and Vater's papilla*. Arch. Chir. Neerlandicum 5, 1, 31. 1953.

The author reports on the therapeutic results in 28 cases of obstructive jaundice due to tumors in the



region of the head of the pancreas and Vater's papilla. Pancreatico-duodenectomy was carried out in five out of eight cases of tumors of the papilla Vateri. Transduodenal excision was carried out in two cases, one of which was for benign papilloma. Carcinoma of the head of the pancreas was invariably treated by palliative operations.

Pancreatico-duodenectomy offers a reasonable chance of cure or increase of the expectation of life in carcinoma of Vater's papilla. Transduodenal excision, though less radical, is necessary in certain circumstances. Carcinoma of the head of the pancreas has such malignant properties that "radical" operation hardly ever leads to recovery. Pancreatico-duodenectomy should be resorted to only in apparently favourable cases. Various forms of entero-biliary anastomosis generally exert a satisfactory palliative effect. Long-term prognosis, however, is very gloomy. If the possibility of obstruction by a tumor cannot be excluded with certainty, laparotomy should be carried out immediately.

Franz J. Lust.

MASUDA, HISAYUKI; OHARA, MITSUO AND KAT-SURA, SHIGEAKI: *Response of the intragastric temperature to various drugs*. Tohoku J. Experimental Med. 57, 2-3, 129, 137. Febr. 1953.

These are the fifth and sixth reports of the authors on their studies of the temperature of the gastrointestinal tract. The response of the intragastric temperature of healthy men to subcutaneous injections of histamine, adrenaline, pilocarpine and atropine was studied simultaneously with those of the axillary temperature, pulse, blood pressure and gastric juice. It was found: 1) The intragastric temperature drops by the four drugs. 2) The drop by histamine is transient, contrary to those by adrenaline and pilocarpine. The drop by atropine is preceded by a slight rise. 3) The maximum drop is large by histamine and pilocarpine, small by adrenaline and atropine. 4) The onset of the drop is more rapid by histamine, slowest by atropine. 5) The change in the axillary temperature is generally parallel with that inside the stomach. 6) Change in the pulse rate is in intimate relation with that in the intragastric temperature. Blood flow is one of the most important factors in the change in the intragastric temperature. 7) By histamine and pilocarpine, which strongly stimulates the gastric secretion, the intragastric temperature is intensely lowered.

The response to subcutaneous injection of benzy-limidazole, to intravenous injection of the same drug and tetraethylammonium bromide was studied. The intragastric temperature drops by the two just mentioned drugs. The drop by histamine is the greatest and both the onset and the recovery are the most rapid. The change in intragastric temperature is not related with that in the gastric free acidity.

Franz J. Lust.

CLARK, D. H.: *Peptic ulcer in women*. Brit. Med. J., June 6, 1953, 1254-1257.

In chronic peptic ulcer in women (both gastric and duodenal) there is relief of symptoms in 90 percent of pregnancies, but with resumption of symptoms after term. Also, there is exacerbation of symptoms at the

menopause. Whether these phenomena can be attributed to hormonal influences or to the mental state is uncertain. Certainly, there is, during pregnancy, greater hormonal activity than can be accomplished by hormonal therapy. Sandweiss and Bralow and others showed that in spite of much research there is no clear proof of a relationship between the sex hormones and peptic ulcer.

SUMMERS, V. K.: *Myxedema coma*. Brit. Med. J., Aug. 15, 1953, 366-368.

Summers describes 4 cases of myxedema dying in coma. Hypothermia was a constant feature, the rectal or vaginal temperatures ranging from 75 to 91.4° F. The use of thyroid extract, thyroxin or cortisone was of no avail. It appears that such coma with hypothermia, while rare, is absolutely fatal.

STRANG, C. AND WALTON, J. N.: *Carcinoma of body and tail of pancreas*. Ann. Int. Med., 39, 1, 15-37.

A study of 58 cases of pancreatic carcinoma of the body and/or tail, indicates that clinical diagnosis is very difficult, having been made in only 3 cases. The clinical picture, in this series, did not vary significantly with the position of the cancer in the pancreas. Pain, loss of appetite, and weight loss with weakness should lead to early laparotomy, when they cannot be otherwise explained, because cure may result if the neoplasm is detected in an early stage.

BUNTON, G. L.: *Acute appendicitis in infancy and early childhood*. Brit. Med. J., July 11, 1953, 71-73.

Acute appendicitis is uncommon under 5 years of age; nevertheless it does occur. The clinical picture of acute appendicitis in the young is changing, because of the wide-spread use of antibiotics. The latter tend to cause abscess formation and to mask peritonitis, when present. One case at age 3 is presented. (The reviewer once assisted in the removal of a "red-hot" appendix in an infant 24 hours old). In children the association of loose stools is fairly common. Everyone should keep the possibility of appendicitis in mind when dealing with acute abdominal conditions in children.

NISSEN, RUDOLF: *The surgical treatment of chronic gastric and duodenal ulcers*. Dtsch. Med. Wo. 77, 44.1277, 1952.

There are three kinds of indication for surgical treatment of peptic ulcer: the absolute, the relative and the economic indication. Free perforation, profuse bleeding, stenosis and malignant change are considered "absolute" indication.

In the second part of his paper the author reviews the late results of different procedures. He considers gastroenterostomy a poor method, followed by a high percentage of gastrojejunal ulcerations.

Vagal resection should be performed only in cases where local and general condition does not permit gastrectomy. Vagal resection, on the other hand, is

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indicated for the treatment of marginal ulcers, provided a large enough resection has been performed previously. If this is not the case, a wider resection should be added to the vagal resection.

Subtotal gastrectomy is considered the best available method. The ulcer bearing area should always be resected. In the author's hands this was possible in all cases of duodenal ulcer. If the pyloric antrum is left behind, gastrojejunal ulcers occur as frequently as in simple gastroenterostomies.

In the author's series there was a mortality rate of 3.08% in 259 partial gastrectomies, performed between 1932 and 1935. In a later series of 266 cases, in the space of 1941 to 1952, the rate of mortality was reduced to 0.4%. There was no death case in the last 249 subtotal gastrectomies. The immediate postoperative result stands doubtless in reasonable relationship to the benign character of the lesion.

Also the end results indicate the value of partial gastrectomy. Gastrojejunal ulcers occurred in 2-2.5% of the cases. Gastrojejunal ulcers are not a complication of the Billroth I kind of operation, neither is the dumping syndrome which occurs in 8% of the Billroth II method. The Billroth I method is considered the operation of choice, but can unfortunately not be performed in all cases.

In the author's series diet restrictions have only to be kept by 20% out of 90% of patients with good result.

GOULSTON, S.: *Experience with infectious hepatitis at Royal Prince Alfred Hospital (Sydney)*. Med. J. Australia, June 27, 1953, 905-913.

After a study of 83 cases of presumed infectious hepatitis, in which chief emphasis was placed on the two major problems of acute hepatic necrosis and the steady progress of hepatitis to hepatic cirrhosis, Goulston wonders in what way further investigations will shed light on these unsolved problems. He believes that further study of the intra-hepatic circulation is very important. Like others, he feels that rest is indispensable in treatment and suggests that the current practice of early ambulation is probably out of place in this disease.

BARGEN, J. A.: *Disease of the liver associated with ulcerative colitis*. Ann. Int. Med., 39, 2, Aug. 1953, 285-288.

Bargen notes that the question of the relation between ulcerative colitis and hepatitis or, later, between ulcerative colitis and cirrhosis, comes up frequently. In some of the patients with both ulcerative colitis and hepatitis, there is little doubt that the hepatitis results, in some way, from the colitis but, in others, doubt remains. It is rather amazing that this complication does not occur frequently among patients with severe ulcerative colitis. However, it is of such serious moment that further careful study of the problem is indicated. The nutritional deficiencies and bacterial infections so characteristic of ulcerative colitis could theoretically easily produce postnecrotic cirrhosis, and it is occasionally actually found.

STANLEY, B. E. C.: *Prostatic dyspepsia*. Brit. Med. J., Aug. 22, 1953, 423-424.

"Silent prostatism" may present itself with symptoms unrelated to the genito-urinary tract, but rather with symptoms suggestive of gastric cancer or early hepatic cirrhosis. Among 200 patients who underwent prostatectomy, 18 cases of this type were found. The chief symptoms were upper abdominal discomfort or pain, nausea and anorexia, and seemed to be due to varying degrees of renal insufficiency. While urinary symptoms were absent, residual urine usually was found. The moral is that in a patient with unexplained dyspepsia, residual urine should be looked for, with a view to making a diagnosis of "silent prostatism."

BLANCO, H. G.: *The pathology of chronic ulcerative colitis: its treatment with ACTH and cortisone*. LaRevista Clinica, 1953, 3, 15-44.

Blanco was greatly impressed by the good results obtained in chronic ulcerative colitis through the use of ACTH and cortisone, particularly when used early in the disease. Six out of nine cases had good results. Three of the six good cases had no relapse one year after discontinuance of the hormones. ACTH was used in the more severe cases. In general, Blanco's dosages were unusually high, but he reports no unfavorable results. He also used ascorbic acid, B-complex, testosterone, psychotherapy, high protein, high potassium and low sodium diets. The essential amino acids were stressed. He believes that chronic ulcerative colitis is a collagen disease, affecting primarily the submucosa, and compares the pathological changes to those resulting from the use of mineralocorticoids.

PENNERBETHY, G. C.: *Non-penetrating wounds of the abdomen*. Harper Hosp. Bull., II, 4, July-Aug. 1953, 161-165.

After a non-penetrating wound of the abdomen, a careful history is needed. Shock should be combatted at once. Morphine should be withheld till a diagnosis is made. Early operation is vital to recovery. If abdominal pain, spasm and tenderness, with or without nausea, persist six hours, laparotomy is indicated. The author wisely points out that the seeming severity of the injury, or the converse, are no indication of the likelihood of internal serious injury. (The abstractor saw a man kicked in the abdomen by a horse, without serious results, and, on the other hand, a boy with ileal perforation resulting from a small swing-gate striking him lightly in the abdomen.)

OSIUS, E. A.: *Meckel's diverticulum*. Harper Hosp. Bull., II, 4, July-Aug. 1953, 155-160.

Three cases are presented. The first was one of intestinal umbilical fistula, the remains of a Meckel's diverticulum. The second had a serious complication, strangulation of a Meckel's diverticulum in a right inguinal hernia. Finally, an unusually interesting large Meckel's diverticulum is presented. Whenever possible, Meckel's diverticulum should be looked for on opening the abdomen for any other operation. Excision of Meckel's diverticulum is indicated whenever encountered.

### SHOCK CONTROLLED BY LEVOPHED IN WIDE VARIETY OF CONDITIONS

Six of 14 patients recovered from myocardial infarction accompanied by severe shock and other complications, most of them "already in congestive heart failure," following intravenous infusions of Levophed (nor-epinephrine) which elevated blood pressures to normal, according to a report in the *American Journal of Medicine* (Sept., 1953).

The pressor agent was administered to a total of 44 patients in shock, with the blood pressures of 42 rising to normal levels, state Drs. John H. Moyer, James M. Skelton and Lewis C. Mills of Houston, Texas. In addition to the 14 cardiogenic cases, the study covered nine patients in shock caused by overwhelming infections, six with excessive hypotension secondary to medications, and 15 due to postoperative reactions.

Writing in the *Journal of the Philadelphia General Hospital* (4:108, Sept., 1953), another research team cites the wide variety of instances in which Levophed has been effective. The drug's indications are "multiple and include almost every etiologic category of shock," they say, adding that it may be the only effective agent in "neurogenic" shock when plasma and blood volume remain normal.

In shock due to blood loss, Drs. Marvin J. Seven and B. H. Liben state, Levophed may be the effective supplemental tool to blood transfusions in overcoming associated decreased peripheral vascular tone, while blood volume is being returned to normal.

In the study by Moyer and colleagues, all 44 patients failed to respond to adequate treatment with other measures, such as fluid replacement and blood transfusions, the doctors report. With the exception of those with hypotension following medication, the rest of the patients "would have been classified as irreversible shock, if a vasopressor agent had not been available."

Levophed produced "a satisfactory and immediate" pressor response and maintained the blood pressure at desired levels. This was achieved in all but two of the 44 cases in an average of 23 hours.

Commenting on results of the study, the investigators state:

"Levophed is particularly valuable in severe hypotensive states following administration of certain drugs to excessively sensitive individuals. This is probably due to the fact that such a response to medication is a peripheral vascular collapse reaction and is of short duration in most instances.

"So-called postoperative irreversible shock is frequently reversible if the blood pressure is maintained long enough for physiologic recovery of the medullary centers, providing the underlying cause of shock is corrected and patients are given adequate but not excessive amounts of intravenous fluid."

They conclude by calling Levophed a "valuable adjunct in the treatment of shock" due to its pressor response, ability to maintain pressure at desired levels, rapid loss of effect after discontinuing the drug, and freedom from undesirable side effects."

Levophed is supplied by Winthrop-Stearns Inc.

### MISSISSIPPI VALLEY MEDICAL SOCIETY 1954 ESSAY CONTEST

The thirteenth Annual Essay Contest of the Mississippi Valley Medical Society will be held in 1954. The Society will offer a cash prize of \$100.00, a gold medal, and a certificate of award for the best unpublished essay on any subject of general medical interest (including medical economics and education) and practical value to the general practitioner of medicine. Certificate of merit may also be granted to the physician whose essays are rated second or third best. Contestants must be members of the American Medical Association who are residents and citizens of the United States. The winner will be invited to present his contribution before the 19th Annual Meeting of the Mississippi Valley Medical Society to be held at Chicago, Sept. 23, 24, 1954, the Society reserving the exclusive right to first publish the essay in its official publication—the MISSISSIPPI VALLEY MEDICAL JOURNAL (incorporating the RADIOLOGIC REVIEW). All contributions shall be typewritten in English in manuscript form, submitted in five copies, not to exceed 5000 words, and must be received not later than May 1, 1954. The winning essays

in the 1953 contest appear in the January 1954 issue of the MISSISSIPPI VALLEY MEDICAL JOURNAL (Quincy, Ill.).

Further details may be secured from: Harold Swanberg, M.D., Secretary Mississippi Valley Medical Society, 209-224 W. C. U. Building, Quincy, Ill.

### NEW ANTIMALARIAL PLAQUENIL, FOUND EFFECTIVE IN 82 CASES

La Lima, Honduras.—A single oral dose of Plaquenil, a new antimalarial drug in the 4-aminoquinoline group, produced normal temperatures within 24 hours and cleared the blood of parasites within 31 hours, without any toxic effects, according to tests conducted here. A report on the use of Plaquenil, which was developed at the Sterling-Winthrop Research Institute but is not yet available commercially, appears in *The American Journal of Tropical Medicine and Hygiene* (2:805, October 13, 1953).

Plaquenil was administered orally and intravenously to 82 hospitalized Honduran patients, aged seven to 64, reports Dr. Mark T. Hoekenga, from the United Fruit Co. Hospital on the north coast of Honduras. A single oral dose of 1.25 gm. was given to 21 patients with *P. falciparum* infection and to 47 patients with *P. vivax*. An additional 14 cases with *P. falciparum* were treated with 0.36 gm. intravenously, in 500 cc. of normal saline solution.

Rapid clinical improvement was noted following both methods of administration, the article states. Sustained normal temperature in the average case "was attained well within 24 hours and the blood was cleared of parasites in 31 hours."

Two cases with *P. falciparum* infection did not respond to the oral dose and had to be re-treated. A 20-year-old girl with the same infection was the only known relapse among the 82 patients. After being re-treated intravenously three weeks following the initial dose by the same route, there was no further relapse in a six-months follow-up.

No toxic effects were reported in the study. There was no appreciable change in the pulse or arterial blood pressure of patients treated by vein, Dr. Hoekenga observes, adding that no instances were found of dizziness, drowsiness, nausea,

vomiting, or visual disturbance. None of the pregnant patients with severe malnutrition or anemia experienced adverse reactions.

#### LABORATORY ANIMAL GROUP HOLDS 4TH ANNUAL MEETING

The fourth annual meeting of the Animal Care Panel, being held December 2 and 3 at Billings Hospital, University of Chicago, Chicago, Illinois, marks a milestone in progress for a group which is becoming more and more significant every year. For the first time in its four year history, the Animal Care Panel is meeting this year as an incorporated organization.

The Panel was originally created by a small number of professional personnel in charge of laboratory animal quarters because they had no place to come and exchange ideas about laboratory animal care. Besides, the care of laboratory animals by specially trained professional personnel was a fairly new concept. Consequently there was little standardization in the field and an inadequate literature. Through its meetings, and as a result of the interest created by the new group, much has been accomplished in the interlude since its founding, both in improving specific areas of care, and in making a start at establishing high standards for housing, nutrition and sanitation.

The program for the fourth annual meeting is perhaps the best balanced ever presented by the Animal Care Panel. It includes reports on aspects of handling laboratory animals of never ending interest, such as nutrition of laboratory dogs, nutrition of small laboratory animals, and the selection of appropriate animal material for a given investigation. Other reports on the program deal with projects of particular timeliness. These include a report from the Hormel Institute of Austin, Minnesota on the development of miniature pigs for research purposes. The animals being raised by the Hormel breeders weigh less than 70 pounds at maturity. A number of them have already been placed in use in research projects, although the project will continue for several years.

Another interesting paper will deal with a colony of rats maintained germ-free, rodent-free and

parasite-free at Notre Dame's famous Lobund Institute for approximately one year.

Two reports of interest to all research biologists are to be given by Dr. Orson N. Eaton, executive secretary of the newly formed Institute of Animal Resources. Dr. Eaton will describe the program which the Institute of Animal Resources has planned, and also will report on the development of the genetic concept of controlled pure animal strains.

Research scientists will also be

interested in a report by W. Lane-Petter of the Laboratory Animals Bureau on the conduct of animal experimentation in Great Britain. The British have long had licensing laws in effect which are of interest to American scientists in that certain forces in this country are currently agitating for adoption of similar legislation.

The Animal Care Panel has grown in its four years of existence to the point where now several hundred individuals attend its annual sessions. The Panel publishes pro-



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ceedings of each meeting and individual members of the Panel are available for consultation on problems in caring for laboratory animals.

A significant aspect of the Animal Care Panel's program is that it represents the only constructive effort now being made in this country to improve conditions under which laboratory animals are maintained, and this effort is coming from within the scientific community, not from those who would hamstring research by severely limiting it.

All those interested in further information about the Animal Care Panel, or in obtaining copies of the Proceedings, should write to the Secretary, Dr. R. J. Flynn, P. O. Box 299, Lemont, Illinois.

#### FIRST WORLD DIRECTORY OF MEDICAL SCHOOLS PUBLISHED BY WHO

The World Health Organization announced recently the publication of the first *World Directory of Medical Schools* which lists the more than 500 medical teaching institutions now open throughout the world, in 84 countries and territories, and gives essential data about each of these schools.

The information gathered by WHO for this bi-lingual, English and French publication includes the following: date of foundation, administration, academic year, conditions for admission, teaching staff, total enrollment, annual admissions, language of instruction, duration of studies, degrees obtainable, annual number of graduates, and tuition fees.

The International Association of Universities (and its executive organ, the International Universities Bureau) assisted the World Health Organization in compiling the Directory, which is considered to meet a long-felt need and lay the foundation for more complete and more exact succeeding editions.

"The World Health Organization has, from its beginning, been interested in professional educational institutions as the fountainhead of trained health workers, whose task is to pit modern science against the world's health problems," says the introduction to the Directory. "Just as the physician is the key figure in any health or medical programme, so is the medical school the basic





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unit in any study of medical education. The first step towards a better understanding of the many problems inherent in, and associated with, medical education, depends upon information as to how many medical teaching institutions there are, where they are located, how many students they have, and other related facts."

The foreword concludes:

"The World Health Organization wishes to express its gratitude to medical schools and their directive bodies for their kindness and cooperation in furnishing the infor-

mation included in this volume. To the faculties and students of the more than 500 institutions herein listed, the World Health Organization extends its greetings and best wishes for the future."

A cursory examination of the Directory indicates that the USA has the largest number of Medical Schools, 79, followed by the USSR, 61. Japan has 46 Medical Schools, of which 21 have been created since the war. India comes next (34) then the United Kingdom (27), France (25) and Italy (21). These last three countries boast some of

the oldest Medical Schools in existence, such as Cambridge, founded in the XIIth Century, Montpellier (1220), Naples (1224), etc. Early Medical Schools also listed in the WHO Directory include Portugal's famed College of Medicine of Coimbra (1290 and the Escuela de Medicina of Mexico (1578), one of the first to be established in the new world.

#### ANNOUNCING SECOND NATIONAL CONFERENCE ON TRICHINOSIS

Auditorium American Medical Association, 535 North Dearborn St., Chicago, Monday, March 1, 1954

Sponsors: American Dietetic Association, American Medical Association, American Pharmaceutical Association, American Public Health Association, American Society of Clinical Pathologists, American Veterinary Medical Association, Association of State and Territorial Health Officers, Conference of Public Health Veterinarians, International Association of Milk and Food Sanitarians, Michigan Memorial-Phoenix Project, University of Michigan, New York Academy of Medicine, United States Public Health Service.

For further information write to: S. E. Gould, M.D., chairman, Continuing Committee on Trichinosis, Wayne County General Hospital, Eloise, Michigan.

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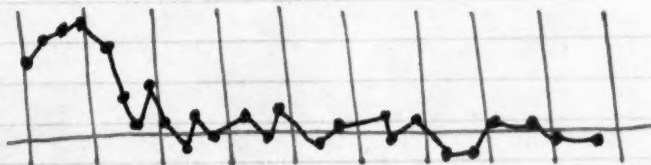
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When the diagnosis is pneumonia, Terramycin therapy usually brings quick results because this broad-spectrum antibiotic is equally effective against coccal, Friedländer's and atypical virus pneumonia.

"After the administration of Terramycin, 59 of the [60] patients...improved rapidly with almost complete defervescence within twenty-four hours."

Given in the recommended daily adult dose of 250 to 500 mg. q. 6 h., Terramycin is exceptionally well tolerated.

"There were no toxic manifestations from this antibiotic....No nausea or vomiting was noted. No patient developed leukopenia."

Even cases that resisted previous treatment with other agents frequently show a gratifying response to Terramycin therapy.

"A case of staphylococcal pneumonia, complicated by tension pneumothorax which had shown no response to [another antibiotic], made a rapid, complete recovery on a dosage of 15 mg. per lb."

1. Knight, V.: New York State J. Med. 50:2173 (Sept. 15) 1950.

2. Potterfield, T. G., and Starkweather, G. A.: J. Philadelphia Gen. Hosp. 2:6 (Jan.) 1951.

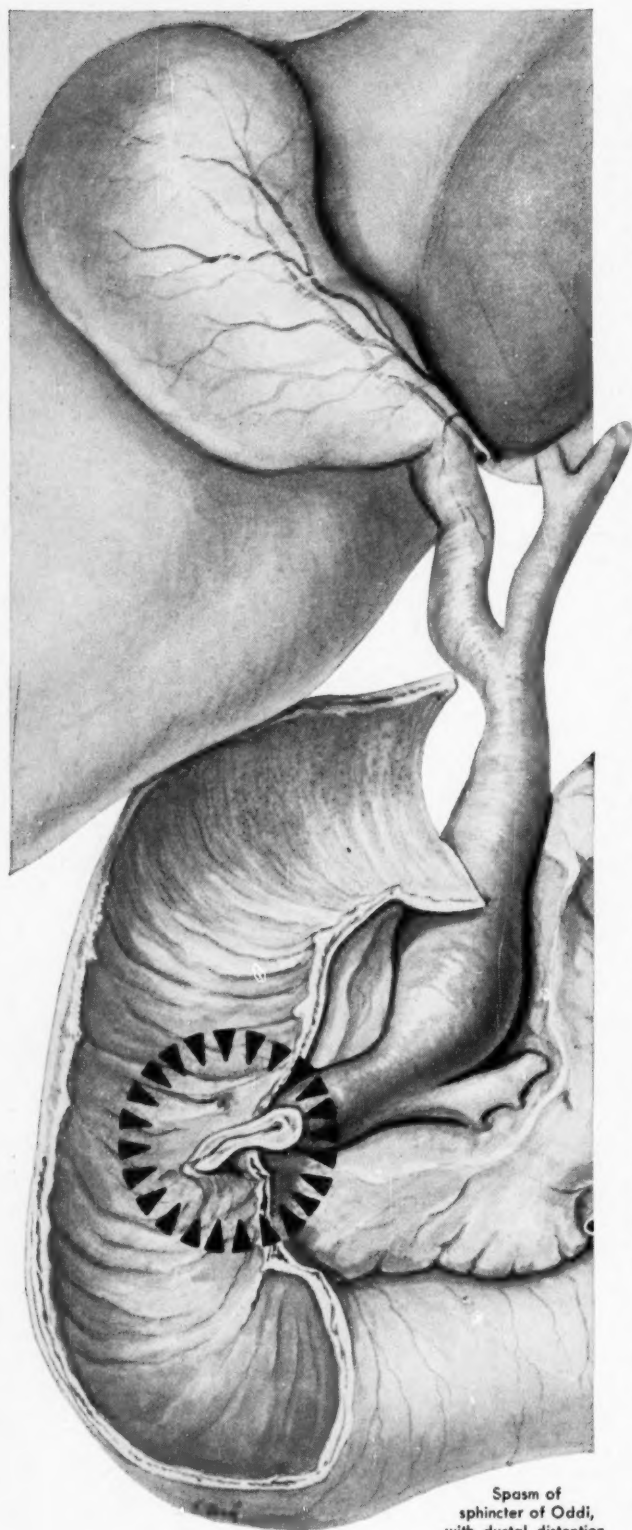
3. Swift, P. N.: Proc. Roy. Soc. Med. 44:1066 (Dec.) 1951.



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Spasm of  
sphincter of Oddi,  
with ductal distention.

## Rational Therapy in Biliary Stasis and Biliary Dyskinesia with Ketochol®

*Ketochol contains all four  
unconjugated bile acids—not salts*

An inadequate flow of bile<sup>1</sup> into the intestine, caused by such conditions as severe liver disease, biliary fistulas, biliary obstruction and congenital atresia of the bile ducts, will eventually produce severe nutritional and digestive disturbances, anemia and a tendency toward abnormal bleeding.

Ketochol stimulates the flow of thin bile to "flush" the biliary passages. Ketochol relieves nausea, vomiting, pain and other symptoms of chronic inflammation of the gallbladder by its hydrocholeretic action.

Ketochol is well tolerated. The average dose is one tablet three times a day with meals, together with a suitable diet.

Ketochol is available in tablet form, 250 mg. (3¾ grains) of ketocholanic acids per tablet.

### Adjunctive Antispasmodic-Sedative Therapy

Pavatrine® with Phenobarbital for selective control of smooth muscle spasm and for mild sedation of the nervous, tense patient is an excellent adjuvant in the management of biliary disorders. The average dose is one or two tablets three or four times daily, as needed.

Pavatrine with Phenobarbital contains 125 mg. (2 grains) of Pavatrine and 15 mg. (¼ grain) of phenobarbital per tablet.

1. Irvin, J. L.: The Secretion and Enterohepatic Circulation of Bile Acids: Replacement of Bile Acids in Biliary Insufficiency, *North Carolina M. J.* 13:206 (April) 1952.

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